08/307,640
12/31/98
DIALOG File
155, 351

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Logging in to Dialog

Trying 9158046...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ********
ENTER PASSWORD:
□a08093fe
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Welcome to DIALOG

Dialog level 98.12.18D

Last logoff:  16dec98 10:17:15
Logon file001 31dec98 15:25:14
ANNOUNCEMENT    ****    ANNOUNCEMENT    ****    ANNOUNCEMENT
NEW
***MediConf (File 431) - December 1, 1998
***French Patents (File 371) - November 2, 1998
                              ***
RELOADED
***BIOSIS Previews (File 5,55)- enhanced 11/16/98, see HELP NEWS5
***Claims Reassignment/Reexamination (File 123)
***Medical Device Register (File 167)
***Healthcare Organizations (File 168)
                              ***
REMOVED
***Hoppenstedt Dir of German Companies to be removed
   effective 12/31/98
***MoneyCenter (MONEY) removed effective 11/1/98
***Financial Times Fulltext (File 622)
                              ***
DIALINDEX
***DIALINDEX categories have been revised. For listing of new/revised
   categories see http://library.dialog.com/bluesheets/html/blo.html.
□dialog
   For more details, see HELP NEWS411.

     >>> Enter.BEGIN HOMEBASE for Dialog Announcements <<<
     >>>    of new databases, price changes, etc.      <<<
***** The DIALORDER suppliers DYNAMIC and FILEDOC are no longer  *****
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File   1:ERIC  1966-1998/Sep
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      Set  Items  Description
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? b 410

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            FTSNET   0.016 Hrs.
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     $0.30  Estimated total session cost   0.092 DialUnits

File 410:Chronolog(R)  1981-1998/Nov/Dec
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? e au=Ferguson, Mark


Ref   Items  Index-term
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E2     9981  JN=CHRONOLOG
E3        1  JN=DIALOG CHRONOLOG
E4       30  PD=198101
E5       42  PD=198102
E6       40  PD=198103
E7       55  PD=198104
E8       37  PD=198105
E9       43  PD=198106
E10      31  PD=198107
E11      41  PD=198108
E12      57  PD=198109

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? b 155, 351

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SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-1998/Dec W4
         (c) format only 1998 Dialog Corporation
  File 351:DERWENT WPI  1963-1998/UD=9851;UP=9848;UM=9846
         (c)1998 Derwent Info Ltd
*File 351: Beginning with UD=9901, UM= and UP= index update codes will
"jump ahead".  See HELP NEWS 351 for details.

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? e au-Ferguson, Mark


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E4        1  AU-GE
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E8          1  AU-NI-CR
E9          1  AU-PHONETIC
E10         1  AU-PLATED
E11         1  AU-PU
E12         1  AU-TI

          Enter P or PAGE for more
? e au=Ferguson, Mark


Ref   Items  Index-term
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E2       22  AU=FERGUSON-SMITH ME
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E9        1  AU=FERGUSSON A B
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E11       1  AU=FERGUSSON A H B
E12       1  AU=FERGUSSON AG

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E5        1  AU=FERGUSON N B
E6        2  AU=FERGUSON N F
E7        1  AU=FERGUSON N S
E8        1  AU=FERGUSON N T
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E12       2  AU=FERGUSON NL

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? s e3

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? e au=ferguson mwj


Ref   Items  Index-term
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E3        0 *AU=FERGUSON MWJ
E4       11  AU=FERGUSON N
E5        1  AU=FERGUSON N B
E6        2  AU=FERGUSON N F
E7        1  AU=FERGUSON N S
E8        1  AU=FERGUSON N T
E9        2  AU=FERGUSON NB
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E11       1  AU=FERGUSON NE
E12       2  AU=FERGUSON NL
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? s s1 and (fibrosis wound)

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          109  S1
        50634  FIBROSIS
       164651  WOUND
S2        27  S1 AND (FIBROSIS OR WOUND)
? rd s2

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
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S3        27  RD S2 (unique items)
? s s3 not py>1992

Processing
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     5435461  PY>1992
S4         9  S3 NOT PY>1992
? t s4/7/1-9


 4/7/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

07348118   93072242
  Sequential changes in histologic pattern and extracellular matrix
deposition during the healing of chronic venous ulcers.
  Herrick SE; Sloan P; McGurk M; Freak L; McCollum CN; Ferguson MW
  Department of Cell, University of Manchester, United Kingdom.
  Am J Pathol (UNITED STATES) Nov 1992, 141 (5) p1085-95, ISSN
0002-9440  Journal Code: 3RS
  Languages: ENGLISH
  Document type: JOURNAL ARTICLE
  As part of a major clinical trial, sequential biopsies were taken from
the margins of venous leg ulcers during their healing. The changing
patterns of tissue architecture and extracellular matrix synthesis during
healing were documented histologically and immunocytochemically. Initial
biopsies were similar in appearance: prominent fibrin cuffs, variable
inflammation, hemosiderin, and red blood cell extravasation. So called
"fibrin cuffs" were highly organized structures composed of laminin,
fibronectin, tenascin, and collagen as well as trapped leukocytes and
fibrin. Fibronectin was absent from the ulcer tissue although collagen was
abundant. Major histologic changes were observed after 2 weeks' pressure
bandage therapy; hemosiderin, acute inflammation, and granulation tissue
with the deposition of fibronectin had all increased and epithelial
migration had commenced. Complete epithelialization was frequent by the
fourth week of treatment, but the basement membrane was incomplete. At this
time, hemosiderin and red blood cell extravasation had decreased and
"fibrin cuffs" were virtually absent although chronic inflammation
remained. The complex organization of the so-called "fibrin cuffs" may
inhibit angiogenesis (but offer protection against increased venous
pressure) in addition to their previously ascribed role in causing tissue
ischemia.


 4/7/2     (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

07312872   92114566
  Control of scarring in adult wounds by neutralising antibody to
transforming growth factor beta.
  Shah M; Foreman DM; Ferguson MW
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Department of Cell and Structural Biology, School of Biological Sciences, University of Manchester, UK.
Lancet (ENGLAND) Jan 25 1992, 339 (8787) p213-4, ISSN 0140-6736
Journal Code: L0S
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Adult wounds heal with scar-tissue formation, whereas fetal wounds heal without scarring and with a lesser inflammatory and cytokine response. We injected the margins of healing dermal wounds in adult rats with neutralising antibody (NA) to transforming growth factor-beta (TGF-beta). All control wounds (irrelevant antibody, or TGF-beta, or no injection) healed with scarring, whereas the NA-treated wounds healed without scar-tissue formation; NA-treated wounds had fewer macrophages and blood vessels, lower collagen and fibronectin contents, but identical tensile strength and more normal dermal architecture than the other wounds. Early manipulation of the concentrations of selected cytokines may be a new approach to the control of scarring.

4/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07012562 92174823
The extracellular matrix of lip wounds in fetal, neonatal and adult mice.
Whitby DJ; **Ferguson MW**
Department of Cell and Structural Biology, School of Biological Sciences, University of Manchester, UK.
Development (ENGLAND) Jun 1991, 112 (2) p651-68, ISSN 0950-1991
Journal Code: ECW
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Wound healing in the fetus occurs rapidly, by a regenerative process and without an inflammatory response, resulting in complete restitution of normal tissue function. By contrast, in the adult, wounds heal with scar formation, which may impair function and inhibit further growth. The cellular mechanisms underlying these differing forms of **wound** healing are unknown but the extracellular matrix (ECM), through its effects on cell function, may play a key role. We have studied the ECM in upper lip wounds of adult, neonatal and fetal mice at days 14, 16 and 18 of gestation. The spatial and temporal distribution of collagen types I, III, IV, V and VI, fibronectin, tenascin, laminin, chondroitin and heparan sulphates were examined immunohistochemically. Results from the fetal groups were essentially similar whilst there were distinct differences between fetus, neonate and adult. Fibronectin was present at the surface of the **wound** in all groups at 1 h post-wounding. Tenascin was also present at the **wound** surface but the time at which it was first present differed between fetus (1 h), neonate (12 h) and adult (24 h). The time of first appearance paralleled the rate of **wound** healing which was most rapid in the fetus and slowest in the adult. Tenascin inhibits the cell adhesion effect of fibronectin and during development the appearance of tenascin correlates with the initiation of cell migration. During **wound** healing the appearance of tenascin preceded cell migration and the rapid closure of fetal wounds may be due to the early appearance of tenascin in the **wound** . Collagen types I, III, IV, V and VI were present in all three **wound** groups but the timing and pattern of collagen deposition differed, with restoration of the normal collagen pattern in the fetus and a scar pattern in the adult. This confirms that lack of scarring in fetal wounds is due to the organisation of collagen within the **wound** and not simply lack of collagen formation. The distribution of chondroitin sulphate differed between normal fetal and adult tissues and between fetal and adult wounds. Its presence in the fetal **wound** may alter collagen fibril formation. No inflammatory response was seen in the fetal wounds. The differences in the ECM of fetal and adult wounds suggests that it may be possible to alter the adult **wound** so that it heals by a fetal-like process without scar formation, loss of

tissue function or restriction of growth.

4/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07007827 92042355
Rapid epithelialisation of fetal wounds is associated with the early deposition of tenascin.
Whitby DJ; Longaker MT; Harrison MR; Adzick NS; **Ferguson MW**
Department of Cell and Structural Biology, School of Biological Sciences, University of Manchester, UK.
J Cell Sci (ENGLAND) Jul 1991, 99 (Pt 3) p583-6, ISSN 0021-9533
Journal Code: HNK
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Wound healing is a complex process involving the interaction of many cell types with the extracellular matrix (ECM). Fetal skin **wound** healing differs from that in the adult in that it occurs rapidly and without scar formation. The mechanisms underlying these differing processes may be related to the fetal environment, the stage of differentiation of the fetal cells or the ECM deposited in the **wound**. The spatial and temporal distribution of two components of the ECM, fibronectin and tenascin, were studied by immunostaining of cryosections from trunk wounds of fetal and adult sheep. Epithelialisation was complete earlier in the fetal **wound** than in the adult. The distribution of fibronectin was similar in fetal and adult wounds but tenascin was present earlier in the fetal **wound**. Fibronectin has several roles in **wound** healing including acting as a substratum for cell migration and as a mediator of cell adhesion through cell surface integrins. The attachment of fibroblasts to fibronectin is inhibited by tenascin and during development the appearance of tenascin in the ECM of migratory pathways correlates with the initiation of cell migration. Similarly, the appearance of tenascin in healing wounds may initiate cell migration. Tenascin was present in these wounds prior to cell migration and the rapid epithelialisation of fetal wounds may be due to the early appearance of tenascin in the **wound**.

4/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06769646 91348403
Immunohistochemical localization of growth factors in fetal **wound** healing.
Whitby DJ; **Ferguson MW**
Department of Cell and Structural Biology, School of Biological Sciences, University of Manchester, United Kingdom.
Dev Biol (UNITED STATES) Sep 1991, 147 (1) p207-15, ISSN 0012-1606
Journal Code: E7T
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Fetal **wound** healing occurs rapidly, in a regenerative fashion, and without scar formation, by contrast with adult **wound** healing, where tissue repair results in scar formation which limits tissue function and growth. The extracellular matrix deposited in fetal wounds contains essentially the same structural components as that in the adult **wound** but there are distinct differences in the spatial and temporal distribution of these components. In particular the organization of collagen in the healed fetal **wound** is indistinguishable from the normal surrounding tissue. Rapidity of healing, lack of an inflammatory response, and an absence of neovascularization also distinguish fetal from adult **wound** healing. The mechanisms controlling these differing processes are undefined but growth factors may play a critical role. The distribution of growth factors in healing fetal wounds is unknown. We have studied, by

immunohistochemistry, the localization of platelet-derived growth factor (PDGF), transforming growth factor beta (TGF beta) and basic fibroblast growth factor (bFGF), in fetal, neonatal, and adult mouse lip wounds. TGF beta and bFGF were present in neonatal and adult wounds, but were not detected in the fetal wounds, while PDGF was present in fetal, neonatal, and adult wounds. This pattern correlates with the known effects in vitro of these factors, the absence of an inflammatory response and neovascularization in the fetal **wound**, and the patterns of collagen deposition in both fetal and adult wounds. The results suggest that it may be possible to manipulate the adult **wound** to produce more fetal-like, scarless, **wound** healing.

4/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06697071 91211368
Fetal diaphragmatic wounds heal with scar formation.
Longaker MT; Whitby DJ; Jennings RW; Duncan BW; **Ferguson MW**; Harrison MR; Adzick NS
Fetal Treatment Program, University of California, San Francisco 94143.
J Surg Res (UNITED STATES) Apr 1991, 50 (4) p375-85, ISSN 0022-4804 Journal Code: K7B
Contract/Grant No.: HD 25505, HD, NICHD; GM 27345, GM, NIGMS
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Fetal **wound** healing is fundamentally different from **wound** healing in the adult. Although experimental work in mice, rats, rabbits, monkeys, and sheep has demonstrated that fetal healing occurs without inflammation and scarring, all of these studies have been limited to fetal skin wounds. Whether all fetal tissues heal in a regenerative-like fashion is unknown. Amniotic fluid exposure may play an important role in scarless fetal skin **wound** healing, but the effect of amniotic fluid on fetal mesothelial **wound** healing has not been characterized. To investigate these questions we created bilateral linear diaphragmatic wounds in 100-day gestation fetal lambs (term = 145 days). The right thoracotomy was closed to exclude amniotic fluid. In contrast, the left thoracotomy was fashioned into an Eloesser flap which permitted the left diaphragmatic **wound** to be continually bathed in amniotic fluid. Wounds were harvested after 1, 2, 7, or 14 days and analyzed by light microscopy and immunohistochemistry with antibodies to collagen types I, III, IV, and VI. Whether bathed in or excluded from amniotic fluid, the mesothelial-lined diaphragm healed with scar formation and without evidence of muscle regeneration. Interestingly, diaphragmatic wounds exposed to amniotic fluid were covered by a thick fibrous collagen peel similar to that seen in gastroschisis bowel. These findings indicate that not all fetal tissues share the unique scarless healing properties of fetal skin.

4/7/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06348938 90133348
Studies in fetal **wound** healing, VI. Second and early third trimester fetal wounds demonstrate rapid collagen deposition without scar formation.
Longaker MT; Whitby DJ; Adzick NS; Crombleholme TM; Langer JC; Duncan BW; Bradley SM; Stern R; **Ferguson MW**; Harrison MR
Department of Surgery, University of California, San Francisco 94143-0510.
J Pediatr Surg (UNITED STATES) Jan 1990, 25 (1) p63-8; discussion 68-9, ISSN 0022-3468 Journal Code: JMJ
Contract/Grant No.: PO1 CA44768, CA, NCI
Languages: ENGLISH

Document type: JOURNAL ARTICLE
The mechanisms that underlie the lack of scarring in fetal wounds are unknown, but probably relate to the control of collagen fibrillogenesis. The role of collagen in the fetal **wound** matrix is controversial, and several **wound** implant models have been used to evaluate collagen deposition in fetal wounds. Unfortunately, these models create an artificial **wound** environment and may thereby affect the results. In order to study fetal **wound** collagen deposition in linear wounds without artificially altering the **wound** environment, we applied a highly sensitive immunohistochemical technique that uses antibodies to collagen types I, III, IV, and VI. We found that collagen was deposited in fetal wounds much more rapidly than in adult wounds. **Wound** collagen deposition occurred in a normal dermal and mesenchymal pattern in second and early third trimester fetal lambs. These findings are consistent with the observation that the fetus heals rapidly and without scar formation. In contrast, wounds in late gestation fetal lambs showed some evidence of scar formation. Further studies may suggest ways to alter the adult **wound** so that it heals in a fetal manner.

4/7/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05605479 89361987
Studies in fetal **wound** healing: III. Early deposition of fibronectin distinguishes fetal from adult **wound** healing.
Longaker MT; Whitby DJ; **Ferguson MW**; Harrison MR; Crombleholme TM; Langer JC; Cochrum KC; Verrier ED; Stern R
Department of Surgery, University of California, San Francisco 94143-0506.
J Pediatr Surg (UNITED STATES) Aug 1989, 24 (8) p799-805, ISSN 0022-3468 Journal Code: JMJ
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Wound healing in the fetus proceeds through a series of steps that differ in the fetus and the adult. At each phase of this complex process, there is signaling between the tissue cells and the **wound** microenvironment, signals that are mediated by and through the extracellular matrix. We postulate that these signals occur earlier in fetal wounds, resulting in more rapid repair. To investigate this, we compared the first 24 hours of **wound** healing in the rabbit fetus and adult, using antibodies against key extracellular matrix macromolecular components: laminin, fibronectin, and type-specific collagens I, III, IV, and V. Fibronectin was the first matrix component to be deposited, and was visualized as early as four hours after fetal wounding and 12 hours after adult wounding. There was no evidence of new laminin or collagen deposition in either the fetal or adult wounds at any time point examined. The early deposition of fibronectin, a matrix adhesion molecule that provides a scaffolding for epithelial migration, may underlie the rapid reepithelialization observed in fetal wounds.

4/7/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05148391 88086439
Fracture repair of reptilian dermal bones: can reptiles form secondary cartilage?
Irwin CR; **Ferguson MW**
Department of Anatomy, Queen's University of Belfast.
J Anat (ENGLAND) Jun 1986, 146 p53-64, ISSN 0021-8782 Journal Code: HBB
Languages: ENGLISH
Document type: JOURNAL ARTICLE

The fracture repair of reptilian dermal bones has not previously been reported. Moreover, repair of fractured dermal bones in birds and mammals involves secondary chondrogenesis whereas that of amphibians does not. Therefore an investigation into the repair of fractured reptilian dermal bones could reveal the stage during vertebrate evolution at which the process of secondary chondrogenesis appeared. Experimental incisions were made in the parietal bones of seventeen lizards (3 species) and 2 snakes (1 species). These resulted in a fracture environment of limited vascularity and increased movement--two known stimuli of secondary chondrogenesis in birds and mammals. Re-epithelialisation was rapid and dead bony fragments quickly sequestered. The blood blot was quickly organised into connective tissue, the dural periostea proliferated, osteoblasts differentiated and bony union was effected after 18 days. The width of the fracture gap was the principal variable affecting the chronology of fracture repair. Secondary cartilage was not detected in any specimen, of any species, at any stage of the fracture repair. It therefore appears that the progenitor cells on reptilian dermal bones are not capable of forming secondary cartilage and that this tissue arose comparatively late in vertebrate evolution.

```
? s fibrosis or wound

          50634  FIBROSIS
         164651  WOUND
      S5 214639  FIBROSIS OR WOUND
? s s5 and (TGF? or transforming(w)growth(w)factor?)

         214639  S5
          12433  TGF?
          33623  TRANSFORMING
         548382  GROWTH
        1515477  FACTOR?
          15264  TRANSFORMING(W)GROWTH(W)FACTOR?
      S6   1560  S5 AND (TGF? OR TRANSFORMING(W)GROWTH(W)FACTOR?)
? s s6 and (TGF(w)beta or factor(w)beta)

           1560  S6
          11877  TGF
         409113  BETA
           9102  TGF(W)BETA
         445536  FACTOR
         409113  BETA
          12169  FACTOR(W)BETA
      S7   1366  S6 AND (TGF(W)BETA OR FACTOR(W)BETA)
? s s7 and (TGW(w)beta(w)3 or beta(w)3)

<------User Break------>
u!
? s s7 and (beta3 or beta(w)3)

           1366  S7
            875  BETA3
         409113  BETA
        4438831  3
           4840  BETA(W)3
      S8     64  S7 AND (BETA3 OR BETA(W)3)
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>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
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...completed examining records
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4643605 PY>1993
S10 9 S8 [redacted] PY>1993
? t s10/7/1-9

10/7/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07710503 94103876
TGF-beta s and **TGF-beta** type II receptor in human epidermis: differential expression in acute and chronic skin wounds.
Schmid P; Cox D; Bilbe G; McMaster G; Morrison C; Stahelin H; Luscher N; Seiler W
Ciba-Geigy Ltd., Pharma Division, Biotechnology, Basel, Switzerland.
J Pathol (ENGLAND) Nov 1993, 171 (3) p191-7, ISSN 0022-3417
Journal Code: JLB
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Exogenously applied **transforming** growth **factor-beta** (**TGF-beta**) isoforms enhance **wound** healing processes in animal models; however, little is known about the expression of endogenous **TGF-beta** s and **TGF-beta** receptors in intact human skin or during **wound** healing. The present study has revealed several unexpected findings by means of in situ hybridization and immunohistology techniques. In humans, **TGF-beta 3** is constitutively expressed in the epidermis of intact skin and in that of acute and chronic wounds--a pattern of expression closely mirrored by the **TGF-beta** type II receptor. Although not detected in intact skin, **TGF-beta** 1 mRNA expression was observed in the regenerating epidermis of acute (thermal) wounds but was not found in chronic decubital (pressure) wounds. **TGF-beta** 2 mRNA expression was not detected in the epidermis of any human skin or **wound** biopsies. From these findings we suggest that constitutive expression of **TGF-beta 3** is important for maintenance of epidermal differentiation and that an induction of **TGF-beta** 1 expression is essential for re-epithelialization of human skin wounds. Lack of **TGF-beta** 1 expression in chronic pressure wounds may be associated with their protracted healing tendencies.

10/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07604313 93365093
Rapid induction and clearance of **TGF beta** 1 is an early response to wounding in the mouse embryo.
Martin P; Dickson MC; Millan FA; Akhurst RJ
Department of Anatomy and Developmental Biology, University College, London, England, UK.
Dev Genet (UNITED STATES) 1993, 14 (3) p225-38, ISSN 0192-253X
Journal Code: DEG
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The **TGF beta** family of growth factors has been implicated as playing a significant role in many aspects of embryonic morphogenesis, and also as a mediator of adult tissue repair processes. Unlike the situation in the adult, tissue repair in the embryo does not result in scarring, and it has been suggested that this might be due, in part, to reduced levels of growth factors, particularly **TGF beta**, at the **wound** site.
We have examined the expression patterns of **TGF beta** genes following wounding of limb bud lesions in cultured E11.5 mouse embryos. The timetable of **wound** closure was investigated by standard light and electron microscopy from the time of wounding until the lesion had re-epithelialised 24 hours later. The expression of transcripts for each of

the three **TGF beta** genes was examined at various time points during the healing process using radioactive in situ hybridisation to tissue sections and wholemount non-radioactive in situ hybridisation to embryo pieces. Within 1 to 3 hours of wounding, transcripts encoding **TGF beta** 1 were rapidly induced within the epithelial cells of the **wound** margin, particularly those cells at the ventral aspect of the **wound**. By 3 to 6 hours post-wounding, **TGF beta** 1 transcripts were detectable in the mesenchyme of the **wound** bed. No **TGF beta 3** induction was observed, and possible **TGF beta** 2 induction was largely obscured by endogenous expression associated with pre-cartilage mesenchymal condensation. Immunocytochemical analysis of tissue sections of the **wound** demonstrated a rapid induction of **TGF beta** 1 protein within 1 hour post-wounding, but also a subsequent rapid clearance of the protein from the **wound** site such that, by 18 hours post-wounding, **TGF beta** 1 levels had returned to near background. These data are discussed in terms of the molecular mechanisms underlying embryonic **wound** healing and the significance of the results to an understanding of scarring following adult tissue repair.

10/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07589924 93343194

Spatial and temporal patterns of immunoreactive **transforming** growth **factor beta** 1, beta 2, and **beta 3** during excisional **wound** repair.

Levine JH; Moses HL; Gold LI; Nanney LB
Department of Surgery, Vanderbilt University, School of Medicine, Nashville, Tennessee 37232.

Am J Pathol (UNITED STATES) Aug 1993, 143 (2) p368-80, ISSN 0002-9440 Journal Code: 3RS
Contract/Grant No.: CA42572-06, CA, NCI; CA49507-03, CA, NCI; GM40437, GM , NIGMS
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Transforming growth **factor beta** (**TGF-beta**) regulates cellular growth and differentiation and stimulates the synthesis and secretion of protein constituents of the extracellular matrix. Three isoforms of **TGF-beta** have been found in mammals. Although the biological activities of **TGF-beta** 1, **TGF-beta** 2, and **TGF-beta 3** are similar at the level of cell culture, distinct in vivo functions for these molecules are emerging. To gain insight into the role of each isoform in **wound** repair, antibodies specific for each isoform of **TGF-beta** were used to examine excisional **wound** repair. Marked differences in the temporal and spatial relationships for immunoreactive **TGF-beta** 1, -beta 2, and -**beta 3** were noted throughout the repair process. **TGF -beta** 2 and **TGF-beta 3** were prevalent by 24 hours after excisional wounding, and strong immunoreactivity was observed in the migrating epidermis. Subtle changes in immunoreactivity occurred for **TGF-beta** 2 and **TGF-beta 3** in cells of the epidermal appendages, mesenchymal derivatives, granulation tissue, and the underlying dermis throughout **wound** repair. In contrast, **TGF-beta** 1 was not associated with any undifferentiated cells and was not present in the dermis and most dermal structures in both nonwounded skin or wounds until day 5 after wounding, when re-epithelialization was complete. Following re-epithelialization, **TGF-beta** 2 and **TGF-beta 3** were present in all four layers of stratum corneum of the differentiating epidermis. All three **TGF-beta** isoforms were present in mesenchymal cells and basal lamina, suggesting their role in the modulation of dermal-epidermal interaction during **wound** repair. Our observations support individual in vivo function for **TGF-beta** isoforms in cutaneous **wound** repair.

10/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07582120 93326149
Injury induced expression of **TGF-beta** 1 mRNA is enhanced by exogenously applied **TGF-beta** S.
Schmid P; Kunz S; Cerletti N; McMaster G; Cox D
CIBA-GEIGY Ltd, Pharma Division, Basel.
Biochem Biophys Res Commun (UNITED STATES) Jul 15 1993, 194 (1) p399-406, ISSN 0006-291X Journal Code: 9Y8
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We have analysed and compared, by in situ hybridisation, the effects of exogenously applied **TGF-beta** s on expression of endogenous **TGF-beta** mRNAs in partial thickness thermal wounds in old and young mice. Although injury induced the expression of **TGF-beta** 1 mRNA in the epidermis and dermis at the **wound** margins, expression of **TGF-beta** 2- or **TGF-beta** 3-mRNA was not detected. Biopsies taken 24 hours following injury revealed a focally clustered distribution of **TGF-beta** 1 hybridisation signals in the dermis, the number of positive cells and expression levels being reduced in old mice. Topical application of all three **TGF-beta** isoforms enhanced **TGF-beta** 1 mRNA expression in the dermis of old and young mice. In biopsies taken three days following injury, **TGF-beta** 1 hybridisation signals were most prominent in the regenerating epidermis although at this timepoint differences in expression levels between treated and non-treated animals were less pronounced.

10/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07518606 93222704
Platelet alpha-granules.
Harrison P; Cramer EM
Rayne Institute, St. Thomas' Hospital, London, UK.
Blood Rev (SCOTLAND) Mar 1993, 7 (1) p52-62, ISSN 0268-960X Journal Code: BLR
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Platelets contain a vast number of biologically active molecules within cytoplasmic granules which are classified according to their respective distinct ultrastructures, densities and content. The alpha-granule is a unique secretory organelle in that it exhibits further compartmentalization and acquires its protein content via two distinct mechanisms: (1) biosynthesis predominantly at the megakaryocyte (MK) level (with some vestigial platelet synthesis) (e.g. platelet factor 4) and (2) endocytosis and pinocytosis at both the MK and circulating platelet levels (e.g. fibrinogen (Fg) and IgG). The currently known list of alpha-granular proteins continues to enlarge and includes many adhesive proteins (e.g. Fg, von Willebrand factor (vWf) and thrombospodin (TSP)), plasma proteins (e.g. IgG and albumin), cellular mitogens (e.g. platelet derived growth factor and **TGF beta**), coagulation factors (e.g. factor V) and protease inhibitors (e.g. alpha 2-macroglobulin and alpha 2-antiplasmin). More recently the inner lining of the alpha-granule unit membrane has been demonstrated to contain a number of physiologically important receptors including glycoprotein IIb/IIIa (alpha IIb **beta 3**) and P-selectin. The alpha-granules originate from small precursor granules which can be observed budding from the trans-Golgi network within the platelet precursor cell the MK. During MK maturation the alpha-granules become very prominent and are ultimately packaged into platelets during thrombopoiesis. The alpha-granular contents are destined for release during

platelet activation at sites of vessel wall injury and thus play an important role in [redacted]emostasis, inflammation, ultim[redacted] **wound** repair and in the pathogenesis of atherosclerosis. (138 Refs.)

10/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07480598 93142865
Involvement of **transforming** growth **factor-beta** in the formation of fibrotic lesions in carcinoid heart disease.
Waltenberger J; Lundin L; Oberg K; Wilander E; Miyazono K; Heldin CH; Funa K
Ludwig Institute for Cancer Research, Biomedical Center, Uppsala, Sweden.
Am J Pathol (UNITED STATES) Jan 1993, 142 (1) p71-8, ISSN 0002-9440 Journal Code: 3RS
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Carcinoid heart disease is a complication of a neuroendocrine carcinoid tumor. Morphologically, it is characterized by the formation of fibrotic plaques with deposition of extracellular matrix in the subendocardium, frequently causing heart valve dysfunction and cardiac failure. Because members of the **transforming** growth **factor-beta** (**TGF -beta**) family are known to stimulate fibroblasts in their production of extracellular matrix, we investigated the expression of the three isoforms of **TGF-beta** and the binding protein for latent **TGF-beta** 1 (LTBP) in carcinoid plaques of the right side of the heart, as well as from control tissue, using immunohistochemistry. Tissue specimens were obtained intraoperatively from nine consecutive patients undergoing valve replacement surgery. **TGF-beta** 1 and **TGF-beta 3** were detected in the fibroblasts of all plaques analyzed, whereas **TGF-beta** 2 was only rarely expressed. The localization of LTBP was partly concordant with that of **TGF-beta** 1, but the positive staining for LTBP was extracellular. Sections from unaffected heart tissue contained few fibroblasts in the subendocardium, showing only weak or no immunostaining for **TGF-beta** 1, -beta 2, and **-beta 3** and no staining for LTBP. These results suggest that **TGF-beta** may play a role in the proliferation of fibroblasts and their matrix production in carcinoid heart lesions.

10/7/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07349717 93107746
Expression and modulation of the vitronectin receptor on human dermal microvascular endothelial cells.
Swerlick RA; Brown EJ; Xu Y; Lee KH; Manos S; Lawley TJ
Department of Dermatology, Emory University, Atlanta, GA 30322.
J Invest Dermatol (UNITED STATES) Dec 1992, 99 (6) p715-22, ISSN 0022-202X Journal Code: IHZ
Contract/Grant No.: RO1 AR 36632, AR, NIAMS
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Microvascular endothelial cells express a variety of cell-surface integrins in vivo and in vitro with varying affinities for matrix proteins. The vitronectin receptor (VnR), a complex of the alpha v and **beta 3** integrin chains, is capable of binding to a variety of matrix proteins that are deposited in injured tissues, including vitronectin, fibrinogen, and thrombin. Staining of frozen sections of human skin with antibodies recognizing the VnR and examination by immunofluorescence microscopy demonstrates staining in a vascular pattern suggesting in vivo expression of the vitronectin receptor on endothelial cells. Examination of

pure cultures of human dermal microvascular endothelial cells (HDMEC) by flow-cytometric analysis and enzyme-linked immunosorbent assay confirmed that HDMEC also express cell surface VnR complex in vitro. Stimulation of human dermal microvascular endothelial cells in vitro with agents that stimulate protein kinase C resulted in dose- and time-dependent increases in expression of alpha v and **beta 3** integrin chains. Additionally, stimulation with basic fibroblast growth factor induced similar increases, but stimulation with **transforming** growth **factor-beta** or interleukin-1 alpha failed to increase VnR expression. Increases in cell-surface VnR expression also correlated with an increased ability of microvascular endothelial cells to bind to vitronectin, but not fibronectin-coated surfaces. Although increases in cell-surface expression of **beta 3** paralleled increases in expression of cell-surface alpha v, regulation of mRNA expression was distinct for each chain. These data suggests that microvascular endothelial cells express the VnR complex in vivo, that the cell-surface expression of this integrin on dermal microvascular endothelial cells can be regulated, and that this regulation may be important in cell adherence, cell migration, and **wound** healing.

10/7/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07116582 92340676
Dog mastocytoma cells produce **transforming** growth **factor beta** 1.
Pennington DW; Lopez AR; Thomas PS; Peck C; Gold WM
Department of Medicine, University of California, San Francisco 94143.
J Clin Invest (UNITED STATES) Jul 1992, 90 (1) p35-41, ISSN 0021-9738 Journal Code: HS7
Contract/Grant No.: HL-07697, HL, NHLBI; HL-24136, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Transforming growth **factor-beta** (**TGF beta**) promotes deposition of extracellular matrix and is associated with fibrotic conditions both in experimental animals and in humans. Although a role for mast cells has been suspected in the pathogenesis of **fibrosis**, no potent mediator capable of stimulating fibroblast growth or extracellular matrix deposition has been identified in mast cell supernatants. We report here the constitutive production of **TGF beta** 1 by four dog mastocytoma cell lines. **TGF beta** 1 was identified by characteristic biologic activity, blockade of biologic effect by specific neutralizing antibody, and by recognition of a band with the appropriate migration by western blot. **TGF beta** 1 mRNA, but not **TGF beta** 2 or **TGF beta 3** mRNA, was also produced constitutively by all four cell lines. Quantitation by bioassay revealed baseline **TGF beta** secretion of approximately 1 ng/10(6) cells over 48 h. Stimulation of mastocytoma cells with phorbol ester increased the rate of release of **TGF beta** 1, most markedly in the first 30 min after stimulation, without increasing **TGF beta** 1 mRNA. Dog mastocytoma cells produced **TGF beta** 1 primarily in a latent form, inactive until treated with acid. Both pure **TGF beta** 1 and **TGF beta** -containing mastocytoma cell-conditioned media inhibited mitogenesis and proliferation in dog mastocytoma cell lines, suggesting that mast cell tumor lines would not grow preferentially based on their ability to produce **TGF beta**. These studies may make possible further investigation of the mechanism by which mast cells contribute to the induction of **fibrosis**.

10/7/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06946803 91300936

Effects of **TGF-**[redacted]**s** in the liver: cell prolife[redacted]ion and fibrogenesis.

Fausto N; Mead JE; Gruppuso PA; Castilla A; Jakowlew SB

Department of Pathology, Brown University, Providence, RI 02912.

Ciba Found Symp (NETHERLANDS) 1991, 157 p165-74; discussion 174-7, ISSN 0300-5208 Journal Code: D7X

Contract/Grant No.: CA 23226, CA, NCI; CA 35249, CA, NCI; HD 24455, HD, NICHD

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

TGF-beta 1 is a potent inhibitor of hepatocyte proliferation in vivo and in culture and an inducer of fibrogenesis. It is produced by non-parenchymal cells in normal, regenerating, neoplastic and pre-neoplastic liver. **TGF-beta** 2 and **beta 3** are also found in liver non-parenchymal cells and the amounts of their mRNAs increase during liver regeneration. **TGF-beta** 2 has similar effects to **TGF-beta** 1. Membranes from normal adult rat liver bind **TGF-beta** 1 with kinetics consistent with the presence of a single high affinity binding site; membranes from livers that have been regenerating for 12-72 hours show high affinity binding sites not detected in livers of normal or sham-operated rats. Affinity labelling of membranes from normal and regenerating liver shows two receptor proteins with Mr 85,000 and 65,000. In contrast, a prominent band corresponding to a binding protein of Mr 280,000 is detected in membrane preparations of cultured liver epithelial cells. Although modulation of **TGF-beta** 1 receptors occurs during liver regeneration, it has not been possible to determine which receptor is responsible for the **TGF-beta** 1 effects in hepatocytes. Other studies have demonstrated a significant correlation between **TGF-beta** 1 mRNA expression and various indicators of fibrogenesis in patients with chronic liver disease. Thus in animals and humans **TGF-beta** 1 appears to play a major role in the pathogenesis of **fibrosis** in chronic liver disease. (27 Refs.)

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=> e Fergusson, Mark/in

E#      FILE             FREQUENCY  TERM
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E1      USPAT                    1     FERGUSSON, JEFFREY ROBERT/IN
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E3      USPAT                    0 --> FERGUSSON, MARK/IN
E4      USPAT                    2     FERGUSSON, NICOLA/IN
E5      USPAT                    1     FERGUSSON, ROBERT THOMAS/IN
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E7      USPAT                    1     FERHOLZ, HANS/IN
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=> e Ferguson, Mark/in

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E3      USPAT                    0 --> FERGUSON, MARK/IN
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E5      USPAT                    2     FERGUSON, MARK E/IN
E6      USPAT                    1     FERGUSON, MARK K/IN
E7      USPAT                    1     FERGUSON, MARK S/IN
E8      USPAT                    2     FERGUSON, MARK W J/IN
E9      USPAT                    1     FERGUSON, MARK WILLIAM JAMES/IN
E10     USPAT                    1     FERGUSON, MARVIN D/IN
E11     USPAT                    1     FERGUSON, MATTHEW K/IN
E12     USPAT                    1     FERGUSON, MATTIE M/IN

=> s e8-e9

             2 "FERGUSON, MARK W J"/IN
             1 "FERGUSON, MARK WILLIAM JAMES"/IN
L1           3 ("FERGUSON, MARK W J"/IN OR "FERGUSON, MARK WILLIAM JAMES"/
IN)

=> t l1 1-3


1.  5,662,904, Sep. 2, 1997, Anti-scarring compositions comprising growth
factor neutralizing antibodies; Mark William James Ferguson, et al.,
424/130.1, 145.1; 530/387.1, 388.24, 391.1, 391.7 [IMAGE AVAILABLE]

2.  5,575,237, Nov. 19, 1996, Method of hatching avian eggs; Mark W. J.
Ferguson, 119/6.8, 300, 311 [IMAGE AVAILABLE]

3.  5,520,926, May 28, 1996, Method of using mannose phosphates for the
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treatment of fibrotic disorders; **Mark W. J. Ferguson**, 424/443, 422, 444, 445, 446, 447, 448, 449; 514/23 [IMAGE AVAILABLE]

=> s l1 and TGF?

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          1980 TGF?
L2           2 L1 AND TGF?
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=> s l1 and fibrosis

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          3152 FIBROSIS
L3           2 L1 AND FIBROSIS
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=> s l2 or l3

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L4           2 L2 OR L3
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=> t l4 1-2

1. 5,662,904, Sep. 2, 1997, Anti-scarring compositions comprising growth factor neutralizing antibodies; **Mark William James Ferguson**, et al., 424/130.1, 145.1; 530/387.1, 388.24, 391.1, 391.7 [IMAGE AVAILABLE]

2. 5,520,926, May 28, 1996, Method of using mannose phosphates for the treatment of fibrotic disorders; **Mark W. J. Ferguson**, 424/443, 422, 444, 445, 446, 447, 448, 449; 514/23 [IMAGE AVAILABLE]

=> s l4 and TGF?/clm

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           252 TGF?/CLM
L5           1 L4 AND TGF?/CLM
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=> t l5 fro clm

US PAT NO: 5,662,904 [IMAGE AVAILABLE] L5: 1 of 1
DATE ISSUED: Sep. 2, 1997
TITLE: Anti-scarring compositions comprising growth factor neutralizing antibodies
INVENTOR: **Mark William James Ferguson**, Stockport, England
David Michael Foreman, Chorlton, United Kingdom
Mamta Shah, Withington, United Kingdom
ASSIGNEE: The Victoria University of Manchester, Manchester, England (foreign corp.)
APPL-NO: 08/122,508
DATE FILED: Sep. 27, 1993
PCT-FILED: Mar. 30, 1992
PCT-NO: PCT/GB92/00570
371-DATE: Sep. 27, 1993
102(E)-DATE: Sep. 27, 1993
PCT-PUB-NO: WO92/17206
PCT-PUB-DATE: Oct. 15, 1992
FRN-PRIOR: United Kingdom 9106678 Mar. 28, 1991
INT-CL: [6] A61K 39/395; A61K 39/44; C07K 16/22; C07K 17/04
US-CL-ISSUED: 424/130.1, 145.1; 530/387.1, 388.24, 391.1, 391.7
US-CL-CURRENT: 424/130.1, 145.1; 530/387.1, 388.24, 391.1, 391.7
SEARCH-FLD: 530/387.1, 388.23, 388.22, 389.2, 412; 435/240.27, 70.21; 424/130.1, 143.1, 145.1, 158.1
REF-CITED:

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5,168,051	12/1992	Derynck et al.	435/69.4
5,520,926	5/1996	Ferguson	

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0 433 225	6/1991	European Patent Office	C07K 7/00
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88/05788	8/1988	World Intellectual Property Organization	C07K 15/00
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ART-UNIT: 186
PRIM-EXMR: Toni R. Scheiner
ASST-EXMR: Nancy A. Johnson
LEGAL-REP: Wallenstein & Wagner, Ltd.

ABSTRACT:

A composition for use in the treatment of wounds to inhibit scar tissue formation during healing, comprising an effective amount of an activity-inhibiting growth factor neutralizing agent or agents specific against all **TGF**-.beta., except for **TGF**-.beta..sub.3, and PDGF, together with a pharmaceutically acceptable carrier. A method of preparing the composition and a method of administering the composition to a host suffering from tissue wounding is also disclosed.

28 Claims, No Drawings

US PAT NO: 5,662,904 [IMAGE AVAILABLE] L5: 1 of 1

CLAIMS:

CLMS(1)

We claim:

1. A method of inhibiting scar tissue formation during the healing of wounds, comprising the steps of administering to a host suffering from tissue wounding a growth factor neutralizing antibody specific against a growth factor selected from the group consisting of **TGF**-.beta..sub.1, **TGF**-.beta..sub.2 and PDGF, wherein the antibody neutralizes the stimulation of macrophage infiltration, fibroblast migration, extracellular matrix synthesis or deposition by fibroblasts, in the wound area before the granulation phase in a dosage effective to reduce activity of the growth factor.

CLMS(2)

2. A method according to claim 1, wherein the growth factor neutralizing

antibody is selected from the group consisting of anti-**TGF**-.beta..sub.1 antibody, anti-**TGF**-.beta..sub.2 antibody and anti-PDGF-antibody.

CLMS(3)

3. A method of inhibiting scar tissue formation during the healing of wounds, comprising the steps of administering to a host suffering from tissue wounding a growth factor neutralizing antibody specific against a growth factor selected from the group consisting of **TGF**-.beta..sub.1, **TGF**-.beta..sub.2 and PDGF, wherein the antibody neutralizes the stimulation of macrophage infiltration, fibroblast migration, extracellular matrix synthesis or deposition by fibroblasts, in the wound area during the granulation phase in a dosage effective to reduce activity of the growth factor.

CLMS(4)

4. A method according to claim 3, wherein the growth factor neutralizing antibody is selected from the group consisting of anti-**TGF**-.beta..sub.1 antibody, anti-**TGF**-.beta..sub.2 antibody, and anti-PDGF-antibody.

CLMS(5)

5. A method according to claim 1, wherein the growth factor neutralizing antibody is encapsulated.

CLMS(6)

6. A method according to claim 5, wherein the capsule is degradable by an external stimulus to release the growth factor neutralizing antibody.

CLMS(7)

7. A method according to claim 6, wherein the external stimulus is selected from the group consisting of UV light, in vivo enzymes, ultrasound and heat.

CLMS(8)

8. A method according to claim 1, wherein the growth factor neutralizing antibody is bound to a binding molecule.

CLMS(9)

9. A method according to claim 8, further comprising the step of detaching the binding molecule from the growth factor neutralizing antibody.

CLMS(10)

10. A method according to claim 9 wherein the binding molecule is detached from the growth factor neutralizing antibody by an external stimulus selected from the group consisting of UV light, in vivo enzymes, ultrasound and heat.

CLMS(11)

11. A method according to claim 1, further comprising the step of administering the growth factor neutralizing antibody in a pharmaceutically acceptable carrier.

CLMS(12)

12. A method according to claim 11, wherein the pharmaceutically

acceptable carrier is selected from the group consisting of a neutral sterile cream, gel, [redacted]osol and powder for topical ap[redacted]cation.

CLMS(13)

13. A method according to claim 11, wherein the pharmaceutically acceptable carrier is selected from the group consisting of a sterile solution for injection, irrigation and inhalation.

CLMS(14)

14. A method according to claim 11, wherein the pharmaceutically acceptable carrier comprises a sterile dressing for topically covering a wound.

CLMS(15)

15. A method according to claim 11, wherein the pharmaceutically acceptable carrier is selected from the group consisting of a biopolymer and a polymer for implanting within the wound.

CLMS(16)

16. A method according to claim 1, further comprising the step of administering a fibroblast growth factor with the growth factor neutralizing antibody.

CLMS(17)

17. A method according to claim 3, wherein the growth factor neutralizing antibody is encapsulated.

CLMS(18)

18. A method according to claim 17, wherein the capsule is degradable by an external stimulus to release the growth factor neutralizing antibody.

CLMS(19)

19. A method according to claim 18, wherein the external stimulus is selected from the group consisting of UV light, in vivo enzymes, ultrasound and heat.

CLMS(20)

20. A method according to claim 3, wherein the growth factor neutralizing antibody is bound to a binding molecule.

CLMS(21)

21. A method according to claim 20, further comprising the step of detaching the binding molecule from the growth factor neutralizing antibody.

CLMS(22)

22. A method according to claim 21 wherein the binding molecule is detached from the growth factor neutralizing antibody by an external stimulus selected from the group consisting of UV light, in vivo enzymes, ultrasound and heat.

CLMS(23)

23. A method according to claim 3, further comprising the step of administering the growth factor neutralizing antibody in a pharmaceutically acceptable carrier.

CLMS(24)

24. A method according to claim 23, wherein the pharmaceutically acceptable carrier is selected from the group consisting of a neutral sterile cream, gel, aerosol and powder for topical application.

CLMS(25)

25. A method according to claim 23, wherein the pharmaceutically acceptable-carrier is selected from the group consisting of a sterile solution for injection, irrigation and inhalation.

CLMS(26)

26. A method according to claim 23, wherein the pharmaceutically acceptable carrier comprises a sterile dressing for topically covering a wound.

CLMS(27)

27. A method according to claim 23, wherein the pharmaceutically acceptable carrier is selected from the group consisting of a biopolymer and a polymer for implanting within the wound.

CLMS(28)

28. A method according to claim 3, further comprising the step of administering a fibroblast growth factor with the growth factor neutralizing antibody.

```
=> s transforming growth factor? or (TGF? and cytokin?)

         29932 TRANSFORMING
        144738 GROWTH
        436974 FACTOR?
          1517 TRANSFORMING GROWTH FACTOR?
                 (TRANSFORMING(W)GROWTH(W)FACTOR?)
          1980 TGF?
          5192 CYTOKIN?
L6        1783 TRANSFORMING GROWTH FACTOR? OR (TGF? AND CYTOKIN?)

=> s l6 and (factor beta or factor b)

        260457 FACTOR
        177314 BETA
          1881 FACTOR BETA
                 (FACTOR(W)BETA)
        260457 FACTOR
       1190181 B
          1357 FACTOR B
                 (FACTOR(W)B)
L7         835 L6 AND (FACTOR BETA OR FACTOR B)

=> s l6 and (fibrosis or wound)

          3152 FIBROSIS
        159771 WOUND
L8         772 L6 AND (FIBROSIS OR WOUND)

=> s l8 and (fibrosis/clm or wound/clm)

           258 FIBROSIS/CLM
         39881 WOUND/CLM
L9         154 L8 AND (FIBROSIS/CLM OR WOUND/CLM)
```

=> s l9 and (TGF?/clm or growth factor/clm)

```
          252 TGF?/CLM
        21330 GROWTH/CLM
        26369 FACTOR/CLM
         1307 GROWTH FACTOR/CLM
                ((GROWTH(W)FACTOR)/CLM)
L10        72 L9 AND (TGF?/CLM OR GROWTH FACTOR/CLM)
```

=> s l10 and beta?/clm

```
        36261 BETA?/CLM
L11        39 L10 AND BETA?/CLM
```

=> s l11 and (beta 3 or b3)

```
       177314 BETA
      2373577 3
         3422 BETA 3
                (BETA(W)3)
        16644 B3
L12         9 L11 AND (BETA 3 OR B3)
```

=> t l12 1-9

1. 5,837,258, Nov. 17, 1998, Induction of tissue, bone or cartilage formation using connective tissue growth factor; Gary R. Grotendorst, 424/198.1; 530/399 [IMAGE AVAILABLE]

2. 5,719,120, Feb. 17, 1998, Use of endoglin polypeptides for modifying the regulatory activity of TGF-.beta.; Michelle Letarte, et al., 514/2; 435/69.1; 514/8; 530/350 [IMAGE AVAILABLE]

3. 5,693,610, Dec. 2, 1997, Binding agent for growth factor; Kenichi Matsunaga, et al., 514/8; 530/395 [IMAGE AVAILABLE]

4. 5,693,607, Dec. 2, 1997, Uses of **TGF**-.beta. receptor fragment as a therapeutic agent; Patricia R. Segarini, et al., 514/2; 435/69.1; 514/8 [IMAGE AVAILABLE]

5. 5,662,904, Sep. 2, 1997, Anti-scarring compositions comprising growth factor neutralizing antibodies; Mark William James Ferguson, et al., 424/130.1, 145.1; 530/387.1, 388.24, 391.1, 391.7 [IMAGE AVAILABLE]

6. 5,591,716, Jan. 7, 1997, Beneficial **wound** healing applications of calreticulin and other hyaluronan-associated proteins; John W. Siebert, et al., 514/12; 530/350, 395, 399 [IMAGE AVAILABLE]

7. 5,520,926, May 28, 1996, Method of using mannose phosphates for the treatment of fibrotic disorders; Mark W. J. Ferguson, 424/443, 422, 444, 445, 446, 447, 448, 449; 514/23 [IMAGE AVAILABLE]

8. 5,118,791, Jun. 2, 1992, Biologically active polypeptides based on **transforming growth factor**-.beta.; John P. Burnier, et al., 530/326, 324 [IMAGE AVAILABLE]

9. 5,108,989, Apr. 28, 1992, Method of predisposing mammals to accelerated tissue repair; Edward P. Amento, et al., 514/12, 21 [IMAGE AVAILABLE]

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SYSTEM:OS  - DIALOG OneSearch
  File 154:MEDLINE(R)  1985-1997/May W5
         (c) format only 1997 Knight-Ridder Info
  File  76:Life Sciences Collection  1982-1997/Feb
         (c) 1997 Cambridge Sci Abs
  File  73:EMBASE  1974-1997/Feb W1
         (c) 1997 Elsevier Science B.V.
  File  55:BIOSIS PREVIEWS(R)  1985-1997/Apr W1
         (c) 1997 BIOSIS
  File 351:DERWENT WPI  1981-1996/UD=9714;UA=9711;UM=9705
         (c)1997 Derwent Info Ltd
*File 351: *** YES, TYPEs in KWIC format are FREE! ***
** Reload delayed to mid-April. See HELP NEWS 351 for more info.
  File 357:Derwent Biotechnology Abs  1982-1997/Mar B2
         (c) 1997 Derwent Publ Ltd
  File 358:Current BioTech Abs  1983-1997/Apr
         Royal Soc Chem & DECHEMA

      Set   Items  Description
      ---   -----  -----------
?s wound?

      S1  196363  WOUND?
?s heal?

      S2 1433324  HEAL?
?s composit?

      S3  769082  COMPOSIT?
?s tgf?

      S4   34437  TGF?
?s s1 and s2 and s3 ands 4

>>>Term "ANDS" in invalid position
?s s1 and s2 and s3 and 4



INT CONF
!
?s s1 and s2 and s3 and s4

          196363  S1
         1433324  S2
          769082  S3
           34437  S4
      S5      24  S1 AND S2 AND S3 AND S4
?rd

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
      S6      23  RD (unique items)
?t s6/7/all
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6/7/1 (Item 1 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08885706 97113832
Human granulation-tissue fibroblasts show enhanced proteoglycan gene expression and altered response to TGF-beta 1.
Hakkinen L; Westermarck J; Kahari VM; Larjava H
Department of Periodontology, University of Turku, Finland.
J Dent Res (UNITED STATES) Oct 1996, 75 (10) p1767-78, ISSN 0022-0345 Journal Code: HYV
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Granulation-tissue fibroblasts are phenotypically unique cells that play an important role in wound repair and the development of chronic inflammatory lesions in connective tissue. In the present study, we compared proteoglycan, type I, and type III procollagen gene expression by granulation-tissue fibroblasts from wound and chrónically inflamed tissues with normal gingival fibroblasts. We also analyzed the effect of TGF-beta 1 on proteoglycan mRNA levels and macromolecule production by these cells. One granulation-tissue fibroblast strain that was composed exclusively of alpha-smooth-muscle actin-positive cells (myofibroblasts) expressed strongly elevated basal levels of biglycan, fibromodulin, and versican (the large chondroitin sulphate proteoglycan), as well as type I and III procollagen mRNA. TGF-beta 1 enhanced more potently the expression of types I and III procollagen, biglycan, and versican mRNA by these cells as compared with normal fibroblasts. Other granulation-tissue fibroblast strains, in which about half of the cells expressed alpha-smooth-muscle actin, also showed enhanced proteoglycan and types I and III procollagen expression as compared with normal fibroblasts. These results suggest that alterations in matrix composition during inflammation and wound healing are regulated partly by altered phenotypes of the cells that produce the matrix, and partly by altered responses of these cells to TGF-beta 1.

6/7/2 (Item 2 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08544843 96164297
Modulation of interleukin-1 receptor expression by transforming growth factor-beta in cultured rabbit articular chondrocytes: analysis by reverse transcription-polymerase chain reaction.
Pronost S; Segond N; Macro M; Redini F; Penfornis H; Jullienne A; Moukhtar MS; Pujol JP
Laboratoire de Biochimie du Tissu Conjonctif, CJF INSERM 91-06, Faculte de Medecine, Caen, France.
Osteoarthritis Cartilage (ENGLAND) Sep 1995, 3 (3) p147-55, ISSN 1063-4584 Journal Code: CCO
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Interleukin-1 receptor type I (IL-1RI) expression in cultured rabbit articular chondrocytes (RAC) was studied by reverse transcription-polymerase chain reaction (RT-PCR). A cDNA probe specific for the rabbit IL-1RI gene was constructed using primers derived from the sequence data of the human, murine and chick receptors. Transforming growth factor-beta 1 (TGF beta-1) was shown to transiently increase the level of

expected 900-bp PCR product at 1 h of incubation and decrease the expression at 48 and 72 h with no effect at 24 h. In receptor binding assays using [125I]-IL-1 alpha, TGF beta decreased IL-1R bioactivity at all time points. These results suggest that TGF beta-induced down-regulation of IL-1 RI could be responsible for its ability to antagonize the effect of IL-1 and that TGF beta may have a role in the repair of articular cartilage.

6/7/3 (Item 3 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

07394274 92351297
Independent modulation of enterocyte migration and proliferation by growth factors, matrix proteins, and pharmacologic agents in an in vitro model of mucosal healing.
Basson MD; Modlin IM; Flynn SD; Jena BP; Madri JA
Department of Surgery, Yale University School of Medicine, New Haven, CT 06510.
Surgery (UNITED STATES) Aug 1992, 112 (2) p299-307; discussion 307-8, ISSN 0039-6060 Journal Code: VC3
Contract/Grant No.: F-32-DK-08123, DK, NIDDK; RO1-DK-38063, DK, NIDDK; RO1-HL-28373, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
BACKGROUND. Gastrointestinal mucosa heals by restitution and proliferation. These are difficult to distinguish in vivo. METHODS. Human Caco-2 enterocytes were cultured on matrix proteins (collagen I, laminin, fibronectin) with growth factors (epidermal growth factor [EGF] and transforming growth factor-beta 1 [TGF-beta 1]) and the tyrosine kinase and prostaglandin inhibitors genistein and indomethacin. Healing was modeled by means of monolayer expansion, proliferation by means of 3H-thymidine uptake, and restitution by means of mitomycin-blocked migration. RESULTS. Changing matrix composition failed to alter proliferation, but collagen I stimulated migration more than laminin or fibronectin (laminin/collagen, 68% +/- 2%; p less than 0.05). EGF (30 ng/ml) increased proliferation on both collagen (225% +/- 11% of basal) and laminin (206% +/- 26%) but increased migration only over laminin (210% +/- 17%) (all, p less than 0.05). TGF-beta 1 (200 pg/ml) stimulated migration over laminin (187% +/- 18%, p less than 0.005) but inhibited migration over collagen (89% +/- 3%, p less than 0.01) and did not affect 3H-thymidine uptake. When cultured on laminin, EGF but not TGF-beta 1 altered organization of the alpha 2 integrin subunit. Genistein (100 mumol/L) inhibited basal and EGF-stimulated 3H-thymidine uptake. In addition, it prevented EGF stimulation of replication-blocked migration (81% +/- 10% vs 190% +/- 20% of basal, p less than 0.0001) without altering basal replication-blocked migration. Indomethacin (10(-5) mol/L) did not alter migration but inhibited basal and EGF-stimulated proliferation by 7% +/- 1% (each, p less than 0.005). CONCLUSIONS. Restitution and proliferation appear independently regulated by matrix and growth factors. It may be possible to individually target specific phases of mucosal healing by means of pharmacologic agents.

6/7/4 (Item 1 from file: 76)
DIALOG(R)File 76:Life Sciences Collection

01767151 3529832
Wound healing using IGF-II and TGF
Antoniades, H.N.; Lynch, S.E.
Institute Molecular Biol., Inc., Worcester, MA (USA)
PATENT NUMBER: US 5256644
(1993)
DOCUMENT TYPE: Patent LANGUAGE: ENGLISH
SUBFILE: Medical and Pharmaceutical Biotechnology Abstracts

A method for healing an external wound of a mammal comprising applying to said wound a wound-healing amount of a composition consisting essentially of purified Insulin-like growth factor-II and transforming growth factor beta.

6/7/5 (Item 2 from file: 76)
DIALOG(R)File 76:Life Sciences Collection

01558225 2679315
Wound fluid amino acid concentrations regulate the effect of epidermal growth factor on fibroblast replication.
Gartner, M.H.; Shearer, J.D.; Bereiter, D.F.; Mills, C.D.; Caldwell, M.D.
Box 120 UMHC, Minneapolis, MN 55455, USA
SURGERY. vol. 110, no. 2, pp. 448-456 (1991.)
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: Oncogenes Abstracts; Biochemistry Abstracts Part 3: Amino Acids, Peptides and Proteins

We evaluated the interactions between EGF and AA concentrations found in WF. Wound fibroblasts were cultured in media prepared to mimic the AA concentrations found in WF on days 1, 5, and 10 and in the presence of varying concentrations of EGF. Fibroblasts cultured in all three experimental media showed a dose response to EGF for both tritiated thymidine uptake (proliferation) and AA uptake. The fibroblast proliferation in response to EGF was augmented by the AA composition of day-5 WF. These data show a dose-dependent effect of EGF on fibroblast replication and AA uptake in the absence of serum that is augmented by the particular AA combination found in day-5 WF and suggests that an optimal physiologic AA profile may aid in EGF stimulation of wound fibroblast replication.

6/7/6 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

10087529 EMBASE No: 96280351
TGFbeta, a biological peptide under control: Latent forms and mechanisms of activation
TGFbeta, UN PEPTIDE BIOLOGIQUE SOUS CONTROLE: FORMES LATENTES ET MECANISMES D'ACTIVATION
Feige J.-J.; Quirin N.; Souchelnitskiy S.
Inserm U 244, CEA-Grenoble, biochim regulations cell endocrines, dept biol moleculaire structurale, 17 rue des Martyrs, 38054 Grenoble Cedex 9 France
Medecine/Sciences (France) , 1996, 12/8-9 (929-939) CODEN: MSMSE

ISSN: 0767-0974
LANGUAGES: French SUMMARY LANGUAGES: French; English
Transforming growth factor-betas (TGFbetas) constitute a family of pluripotent regulators of cell growth and differentiation. The three mammalian isoforms of TGFbeta are expressed as latent complexes that need to be converted into active forms before interacting with their ubiquitous receptors. This review provides a summary of some recent advances in the understanding of the biochemical composition of the latent forms of TGFbetas and of the physiological mechanisms of their activation. Three distinct latent complexes have been characterized in the conditioned medium of a variety of cell types: a complex between alpha2-macroglobulin and mature TGFbeta, a non-covalent complex between the pro-region (LAP) and the mature form of TGFbeta and a similar complex containing the additional protein LTBP covalently linked to LAP. The mechanisms for activation of these latent forms in vivo are not fully characterized but may involve processes such as proteolysis and molecular interaction with thrombospondins. Although several other factors have been implicated, the critical step controlling the biological activity of TGFbeta appears to be the activation of the latent molecule. Modulating the level of latent TGFbeta activation by the use of agonists or antagonists of this reaction appears as a possible therapeutic approach for the treatment of auto-immune diseases, arteriosclerosis or wound healing.

6/7/7 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

8438762 EMBASE No: 92115896
The utility of collagen-based vehicles in delivery of growth factors for hard and soft tissue wound repair
McPherson J.M.
USA
CLIN. MATER. (United Kingdom) , 1992, 9/3-4 (225-234) CODEN: CLNME
ISSN: 0267-6605
LANGUAGES: English SUMMARY LANGUAGES: English
Bovine demineralized bone powder and reconstituted bovine dermal collagen have been effectively utilized during the past several years to deliver a variety of growth factors in animal models of hard and soft tissue wound repair. Bone morphogenetic proteins have been delivered in a demineralized bone powder matrix to promote ectopic bone formation in the rat subcutaneous model with the objective of studying the process of endochondral bone formation and evaluating the utility of such factors in promoting repair of hard tissue defects. Reconstituted bovine dermal collagen gels and sponges, including composites of collagen and heparin, have been utilized to deliver growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-beta) and fibroblast growth factor (FGF) to study their effects in subcutaneous and incisional models of dermal wound repair. The results of these experimental animal studies have provided convincing evidence that the rheological properties, biocompatibility and resorbable nature of type I collagen make it an excellent delivery vehicle for evaluation of a variety of growth factors in human clinical studies of hard and soft tissue wound repair.

6/7/8 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI

011167696 WPI Acc No: 97-145621/13
XRAM Acc No: C97-046532
Crystalline form of transforming growth factor beta-3 - useful in compsns. as slow release form of TGF, e.g. for wound healing, and for structure determn. in rational drug design
Patent Assignee: (CIBA) CIBA GEIGY AG
Author (Inventor): ARVINTE T; GRUETTER M; MITTL P
Number of Patents: 001
Number of Countries: 027
Patent Family:

CC Number	Kind	Date	Week	
WO 9705166	A1	970213	9713	(Basic)

Priority Data (CC No Date): EP 95810484 (950725)
Applications (CC,No,Date): WO 96EP3140 (960717)
Language: English
EP and/or WO Cited Patents: 7.Jnl.Ref; US 5322933
Designated States
(National): AU; CA; HU; IL; JP; KR; MX; NO; NZ; US
(Regional): AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT ; SE
Abstract (Basic): WO 9705166 A
A crystalline form of transforming growth factor beta (TGF- beta 3) is new. Also claimed are: (1) pharmaceutical prepns. comprising crystalline TGF- beta , esp. TGF beta 3; (2) a method for the prepn. of crystalline TGF- beta 3, characterised in that the crystallisation buffer comprises soluted TGF- beta 3 and a precipitating agent; and (3) a method for drug design, characterised in that TGF- beta 3 crystals are used for the determination of the structure.
USE - Crystalline TGF beta is useful (i) in slow release compsns. for treatment of conditions such as wounds, oral or intestinal mucositis, osteoarthritis, bone disease and repair, generally wherever TGF is normally used, and (ii) for structure determn. in rational drug design.
ADVANTAGE - Crystalline TGF shows lower tendency than the dissolved protein to adsorb on the walls of vials and is more stable against oxidn.Variation of the properties, e.g. size, of the crystals allows control over the rate at which active TGF is released in vivo.
Dwg.0/0
Derwent Class: A96; B04; D16;
Int Pat Class: A61K-038/18; C07K-014/405

6/7/9 (Item 2 from file: 351)
DIALOG(R)File 351:DERWENT WPI

011064734 WPI Acc No: 97-042659/04
Related WPI Accession(s): 97-042658
XRAM Acc No: C97-013442
Connective tissue growth factor coding sequence and protein - used in the treatment of proliferative disorders and to accelerate wound healing
Patent Assignee: (UYSF-) UNIV SOUTH FLORIDA
Author (Inventor): BRADHAM D M; GROTENDORST G R
Number of Patents: 002
Number of Countries: 069

Patent Family:

CC Number	Kind	Date	Week	
WO 9638172	A1	961205	9704	(Basic)
AU 9659582	A	961218	9714	

Priority Data (CC No Date): WO 96US8140 (960531)
Applications (CC,No,Date): AU 9659582 (960531)
Language: English
EP and/or WO Cited Patents: 2.Jnl.Ref
Designated States
(National): AL; AM; AT; AU; AZ; BB; BG; BR; BY; CA; CH; CN; CZ; DE; DK; EE; ES; FI; GB; GE; HU; IS; JP; KE; KG; KP; KR; KZ; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; TJ; TM; TR; TT; UA; UG; UZ; VN
(Regional): AT; BE; CH; DE; DK; EA; ES; FI; FR; GB; GR; IE; IT; KE; LS; LU; MC; MW; NL; OA; PT; SD; SE; SZ; UG
Filing Details: AU9659582 Based on WO 9638172
Abstract (Basic): WO 9638172 A

An isolated polynucleotide (I) encoding the connective tissue growth factor (CTGF) polypeptide of 349 residues given in the specification, is new. Also claimed are: (1) an isolated polynucleotide having the sequence (II) and sequences complementary to this: GTGTCAAGGGGTC (II) (2) a method for identifying a composition which effects CTGF expression comprising: (a) incubating components comprising the composition and TGF-beta regulatory element (TbetaRE), where the incubation is carried out under conditions and for a time sufficient to allow the components to interact; and (b) measuring the effect of the composition on CTGF expression.

USE - A composition containing the CTGF polypeptide may be used to accelerate wound healing and to ameliorate a cell proliferative disorder (claimed). CTGF inhibitors may be used in the treatment of atherosclerosis, and also in the treatment of various fibrotic diseases (also claimed) including scleroderma, arthritis, alcoholic liver cirrhosis, keloid and hypertrophic scar.

Dwg.0/8

Derwent Class: B04; D16;
Int Pat Class: A61K-038/18; A61K-039/395; C07H-021/04; C07K-016/22

6/7/10 (Item 3 from file: 351)
DIALOG(R)File 351:DERWENT WPI

011064733 WPI Acc No: 97-042658/04
Related WPI Accession(s): 97-042659
XRAM Acc No: C97-013441
Connective Tissue Growth Factor composition - for inducing bone, tissue and cartilage formation and wound healing
Patent Assignee: (GROT/) GROTENDORST G R
Author (Inventor): GROTENDORST G R
Number of Patents: 002
Number of Countries: 069
Patent Family:

CC Number	Kind	Date	Week	
WO 9638168	A1	961205	9704	(Basic)
AU 9658855	A	961218	9714	

Priority Data (CC No Date): WO 96US8140 (960531)

Applications (CC,No,Date): AU 9658855 (960531); WO 96US8210 (960531)
Language: English
EP and/or WO Cited Patents: US 5149691; US 5356630; US 5399361; US 5408040
Designated States
(National): AL; AM; AU; AZ; BB; BG; BR; BY; CA; CN; CZ; EE; FI; GE; HU; IS ; JP; KG; KP; KR; KZ; LK; LR; LS; LT; LV; MD; MG; MK; MN; MX; NO; NZ; PL; RO; RU; SG; SI; SK; TJ; TM; TR; TT; UA; UZ; VN
(Regional): AT; BE; CH; DE; DK; EA; ES; FI; FR; GB; GR; IE; IT; KE; LS; LU ; MC; MW; NL; OA; PT; SD; SE; SZ; UG
Filing Details: AU9658855 Based on WO 9638168
Abstract (Basic): WO 9638168 A

A pharmaceutical compsn. comprising Connective Tissue Growth Factor (CTGF) is new. The compsn. pref. further comprises a suitable carrier, a second growth factor (esp. Transforming Growth Factor-beta, (TGF-beta)) and at least1 collagen.

USE - Compsns. comprising CTGF and a carrier are used for inducing bone formation, e.g. to treat osteoporosis, osteoarthritis and osteochonarytis; for inducing tissue and cartilage formation; and for inducing wound healing (all claimed). The CTGF can be used in ex vivo culture systems, e.g. to expand stem cells or chondrocytes prior to re-implantation.

ADVANTAGE - CTGF is cysteine-rich protein and as such is more stable to protease degradation than Platelet-Derived Growth Factor and other growth factors used in prior art wound healing agents. Inclusion of TGF-beta in the compsn. stimulates endothelial cells and fibroblasts at the site of bone or cartilage formation and wounding to produce endogenous CTGF to augment the exogenous supply.

Dwg.0/8

Derwent Class: B04; D16;
Int Pat Class: A61K-038/18; A61K-038/39; C07K-014/475; C07K-014/495; C07K-014/78

6/7/11 (Item 4 from file: 351)
DIALOG(R)File 351:DERWENT WPI

009674829 WPI Acc No: 93-368382/46
Related WPI Accession(s): 97-033040
XRAM Acc No: C93-163431

Viscous, film-forming, bio-adhesive ointment compsn. - comprises water, mineral oil, poly-alkylene glycol and hydrophilic substd. cellulose

Patent Assignee: (BERL-) BERLEX LAB INC; (BERL-) BERLEX BIOSCIENCES DIV BERLEX LAB INC
Author (Inventor): HSU R; MTIMKULU T; SHAKED Z
Number of Patents: 005
Number of Countries: 020
Patent Family:

CC	Number	Kind	Date	Week	
WO	9321905	A1	931111	9346	(Basic)
AU	9342922	A	931129	9411	
EP	648113	A1	950419	9520	
JP	7508975	W	951005	9548	
AU	670094	B	960704	9634	

Priority Data (CC No Date): US 872755 (920423)
Applications (CC,No,Date): WO 93US3812 (930423); AU 9342922 (930423); EP 93912344 (930423); WO 93US3812 (930423); JP 93519387 (930423); WO

93US3812 (930423); AU 9342922 (930423)
Language: English
EP and/or WO Cited Patents: US 3818105; US 4393061; US 4867970; US 4929422
Designated States
(National): AU; CA; JP
(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE ; LI
Filing Details: AU9342922 Based on WO 9321905; EP0648113 Based on WO 9321905; JP07508975 Based on WO 9321905; AU0670094 Previous Publ. AU 9342922; AU0670094 Based on WO 9321905
Abstract (Basic): WO 9321905 A

Solid aq. mineral oil emulsion ointment compsn. is claimed which is readily spreadable and adapted for topical application and which, when spread on a moist skin or mucosal surface, forms a stable, coherent layer on it which resists removal by water or a body fluid associated with the surface to which it is applied. The compsn. comprises water, mineral oil, an amt. of a polyalkylene glycol (I) and opt. a non-ionic surfactant (II) effective to stabilise the emulsion, and a hydrophilic substd. cellulose (III).

Pref. (I) is a polyethylene glycol, (II) is a polyoxyethylene sorbitan non-ionic surfactant and (III) is hydroxypropyl-methylcellulose (HPMC).

USE/ADVANTAGE - When the compsn. is spread on the skin or a mucosal surface or a wund, lesion or ulcer, it forms a continuous layer which adheres strongly and persistently and resists physical removal and washing off by body fluids. The layer forms a tenacious barrier to the atmosphere which promotes healing and preferential diffusion of pharmaceutically active ingredients into wound tissue rather than into mucosal fluids. The compsns. are excellent vehicles for wound-healing promoters including growth factors such as transforming growth factor-alpha. (TGF-alpha). Dwg.0/0

Derwent Class: A96; B07; P32; B04;
Int Pat Class: A61F-013/00; A61K-009/06; A61K-009/107; A61K-009/70; A61K-037/43
Derwent Registry Numbers: 1870-U; 2044-U

6/7/12 (Item 5 from file: 351)
DIALOG(R)File 351:DERWENT WPI

009643035 WPI Acc No: 93-336584/42
XRAM Acc No: C93-148866
Non-fibrotic growth factor and opt. anti-fibrotic agent compsn. - utilised for stimulating wound healing without fibrosis, also for treating fibrotic disease
Patent Assignee: (UYMA-) UNIV VICTORIA MANCHESTER
Author (Inventor): FERGUSON M W J; SHAH M; SHAH H
Number of Patents: 011
Number of Countries: 008
Patent Family:

CC Number	Kind	Date	Week	
WO 9319769	A1	931014	9342	(Basic)
AU 9337623	A	931108	9408	
NO 9403466	A	940916	9443	
EP 646012	A1	950405	9518	
CZ 9402366	A3	950412	9524	
SK 9401168	A3	950208	9525	

JP 7505378	W	950615	9532
HU T68905	T	950828	9540
NZ 249937	A	960925	9644
AU 673161	B	961031	9651
BR 9306226	A	961203	9703

Priority Data (CC No Date): GB 926861 (920328)
Applications (CC,No,Date): BR 936226 (930322); WO 93GB586 (930322); WO 93GB586 (930322); AU 9337623 (930322); WO 93GB586 (930322); NO 943466 (940916); EP 93906723 (930322); WO 93GB586 (930322); CZ 942366 (930322); SK 941168 (940928); WO 93GB586 ( ); JP 93517193 (930322); WO 93GB586 (930322); WO 93GB586 (930322); HU 942771 (930322); NZ 249937 (930322); WO 93GB586 (930322); AU 9337623 (930322)
Language: English
EP and/or WO Cited Patents: EP 375127; EP 433225; WO 9003810; WO 9110727; WO 9217206
Filing Details: BR9306226 Based on WO 9319769; AU9337623 Based on WO 9319769; EP0646012 Based on WO 9319769; JP07505378 Based on WO 9319769; HU0068905 Based on WO 9319769; NZ0249937 Based on WO 9319769; AU0673161 Previous Publ. AU 9337623; AU0673161 Based on WO 9319769
Abstract (Basic): WO 9319769 A

Healing compsn. (A) contains at least one non-fibrotic growth factor (I) and a pharmaceutically acceptable carrier.

Esp. (I) is transforming growth factor (TGF) beta 3 (Ia) or fibroblast growth factor (Ib) and the compsn. may include an anti-fibrotic agent (II). (I) and (II) can be present in active or inactive form (e.g, in a capsule which can be degraded by UV light, ultrasound, in vivo enzymes or heat).

USE/ADVANTAGE - (A) is used to facilitate repair and healing of wounds without excessive fibrosis and also to treat fibrotic conditions (e.g liver cirrhosis, glomerulonephritis, pulmonary fibrosis, ulcers, etc.). (I) is formulated with a neutral sterile cream, gel, aerosol or powder for topical application; as a patch or dressing; as a sterile soln. for irrigation, injection or inhalation, or as a tablet or capsule. The carrier may also be a biopolymer (e.g collagen or hyaluronic acid) for use as an implant or controlled release system. Dwg.0/0

Derwent Class: B04; D16;
Int Pat Class: A61F-013/00; A61K-009/06; A61K-009/08; A61K-009/12; A61K-009/14; A61K-009/20; A61K-009/22; A61K-009/48; A61K-031/70; A61K-037/02; A61K-037/36; A61K-038/00; A61K-038/18; A61K-038/22; A61K-039/395; C07K-015/00; C07K-016/22

6/7/13 (Item 6 from file: 351)
DIALOG(R)File 351:DERWENT WPI

009473847 WPI Acc No: 93-167388/20
XRAM Acc No: C93-074605

Compsn. contg. platelet derived growth factor - comprises a hydroxyethyl cellulose gel for long-term storage stability for use in wound healing

Patent Assignee: (NOVO) NOVO-NORDISK AS; (ZYMO) ZYMOGENETICS INC
Author (Inventor): EDWARDS M W; LARSEN N C
Number of Patents: 002
Number of Countries: 029

Patent Family:

CC Number	Kind	Date	Week	
WO 9308825	A1	930513	9320	(Basic)
AU 9230623	A	930607	9338	

Priority Data (CC No Date): US 786806 (911104)
Applications (CC,No,Date): WO 92US9431 (921103); AU 9230623 (921103)
Language: English
EP and/or WO Cited Patents: EP 267015; US 5124316; WO 8803409; WO 8905656
Designated States
(National): AU; BG; BR; CA; CS; FI; HU; JP; KR; NO; PL; RO; RU
(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; OA; SE
Filing Details: AU9230623 Based on WO 9308825
Abstract (Basic): WO 9308825 A

Compsn. comprises a therapeutically effective amt. of platelet derived growth factor (PDGF) in a hydroxyethyl cellulose gel. The compsn. may further comprise a preservative, e.g. methyl paraben, ethanol, transforming growth factor (TGF) alpha or beta, epidermal growth factor (EGF), basic or acidic fibroblast growth factor (FGF), platelet factor 4, insulin or a somatomedin. Also claimed is a compsn. comprising P DGF-BB and methyl paraben in a hydroxyethyl cellulose gel.

USE/ADVANAGE - The PDGF is stable over long-term storage in the gel and the compsn. is suitable for topical administration to promote wound healing in conditions e.g. ulcers, superficial wounds and lacerations, abrasions, surgical wounds, burns and bone defects.

In an example, PDGF-BB at 10,200 and 1,000 micro g/ml was formulated into 1.6% (v/v) hydroxyethyl cellulose gels contg. 0.2% (w/v) methyl paraben and 0.68% (w/v) sodium acetate (pH adjusted to 5.5 with HCl). Samples were held for 8 weeks at temps. of 4, 15, 25, 30 and 40 deg.C. The results showed that there was no loss of mitogenic activity and no decomposition of PDGF over the 8 weeks of storage.

Dwg.0/1
Derwent Class: A96; B04; B05;
Int Pat Class: A61K-037/02; A61K-047/38
Derwent Registry Numbers: 0245-U; 0689-U; 1851-U; 1859-U

6/7/14 (Item 7 from file: 351)
DIALOG(R)File 351:DERWENT WPI

009238576 WPI Acc No: 92-365997/44
XRAM Acc No: C92-162476

Compsn. for treating wounds to inhibit scar tissue - contains agent, esp. antibody, which selectively neutralises fibrotic growth factors

Patent Assignee: (UYMA-) UNIV VICTORIA MANCHESTER
Author (Inventor): FERGUSON M W J; FOREMAN D M; SHAH M
Number of Patents: 005
Number of Countries: 035
Patent Family:

CC Number	Kind	Date	Week	
WO 9217206	A1	921015	9244	(Basic)
AU 9214368	A	921102	9305	
EP 585242	A1	940309	9410	
JP 6506205	W	940714	9432	
AU 661840	B	950810	9540	

Priority Data (CC No Date): GB 916678 (910328)
Applications (CC,No,Date): AU 9214368 (920330); WO 92GB570 (920330); AU 9214368 (920330); WO 92GB570 (920330); EP 92907214 (920330); WO 92GB570 (920330); JP 92506944 (920330); WO 92GB570 (920330)
Language: English
EP and/or WO Cited Patents: EP 258817; EP 282317; EP 310176; EP 321095; US 4209832; WO 9110727
Designated States (National): AU; BB; BG; BR; CA; FI; HU; JP; KP; KR; LK; MG; MW; NO; PL; RO ; RU; SD; US
(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LU; MC; NL; OA; SE; LI
Filing Details: AU0661840 Previous Publ. AU 9214368; AU0661840 Based on WO 9217206; AU9214368 Based on WO 9217206; EP0585242 Based on WO 9217206; JP06506205 Based on WO 9217206
Abstract (Basic): WO 9217206 A

Compsn. for treating wounds comprises, apart from an acceptable carrier, an agent (A) which neutralises fibrotic growth factors (but not other growth factors).

More specifically (A) is (1) a neutralising antibody (esp. one directed against TGF (transforming growth factor) beta1 or beta2 or PDGF (platelet-derived growth factor)); (2) a receptor blocking agent (esp. a peptide contg. the appropriate receptor binding site); (3) a cpd. which binds to the growth factor to inhibit receptor binding (esp. docorin or biglycan); (4) an antisense oligonucleotide to growth factor mRNA; (5) a ribozyme active against growth factor mRNA or (6) a soluble form of the receptor (or its binding domain).

USE/ADVANTAGE - The compsn. inhibits scar tissue formation during healing partic. of skin wounds caused by accidents, surgery, etc.. It has no significant effect on healing time or strength of the healed wounds. When the compsn. also contains e.g. fibroblast growth factor, it will also accelerate healing Dwg.0/0

Derwent Class: A96; B04; D22; B07;
Int Pat Class: A61K-031/70; A61K-031/71; A61K-037/02; A61K-037/48; A61K-039/395; A61K-048/00

6/7/15 (Item 8 from file: 351)
DIALOG(R)File 351:DERWENT WPI

009221515 WPI Acc No: 92-348938/42
Related WPI Accession(s): 90-187401
XRAM Acc No: C92-154881

Compsn. comprising new chimeric TGF-B (TGF-beta 1-beta 2) - inhibits proliferation of vascular endothelial cells, useful for treating cancer and to promote wound healing; TRANSFORMING GROWTH FACTOR

Patent Assignee: (BRIM) BRISTOL-MYERS SQUIBB CO
Author (Inventor): MADISEN L; MERWIN J; PURCHIO A F; MERWIN J R
Number of Patents: 009
Number of Countries: 024
Patent Family:

CC Number	Kind	Date	Week	
WO 9216228	A1	921001	9242	(Basic)
ZA 9201850	A	921125	9302	
AU 9218878	A	921021	9303	
PT 100240	A	930730	9334	
EP 575559	A1	931229	9401	
US 5304541	A	940419	9415	

JP 6506470	W	940721	9433
EP 575559	A4	950426	9614
AU 669331	B	960606	9630

Priority Data (CC No Date): US 669171 (910314); US 284972 (881215); US 667246 (910308)
Applications (CC,No,Date): AU 9218878 (920313); WO 92US1993 (920313); ZA 921850 (920312); AU 9218878 (920313); WO 92US1993 (920313); PT 100240 (920313); EP 92910740 (920313); WO 92US1993 (920313); JP 92509951 (920313); WO 92US1993 (920313); EP 92910740 ()
Language: English
EP and/or WO Cited Patents: 2.Jnl.Ref; US 4742003; EP 374044 A
Designated States
(National): AU; CA; FI; JP; KR; NO
(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LU; MC; NL; SE; LI
Filing Details: AU0669331 Previous Publ. AU 9218878; AU0669331 Based on WO 9216228; AU9218878 Based on WO 9216228; EP0575559 Based on WO 9216228; US5304541 CIP of US 5244793; JP06506470 Based on WO 9216228

Abstract (Basic): WO 9216228 A

A pharmaceutical compsn. comprising chimeric transforming growth factor (TGF) beta 1/beta 2 or anti-chimeric TGF beta 1/beta 2 antibody (Ab), is new.

More specifically the sequence of the hybrid TGF, beta 1/beta 1/beta 2 protein, and the corresp. nucleotide sequence, is given in the specification.

USE - The compsn. contg. the hybrid protein is useful for inhibiting the proliferation of vascular endothelial cells and inducing smooth muscle cell migration. The compsn. contg. the hybrid Ab is useful for inhibiting microvascular cell neovascularisation. It is useful for treating cancer and for promoting wound heal Dwg.0/6

Abstract (US): 9415 US 5304541 A

Inhibition of vascular endothelial cell proliferation comprises contacting the cells with chimeric TGF-5-beta.

USE - Used for inducing smooth muscle cell migration. Dwg.0/6

Derwent Class: B04; D16;
Int Pat Class: A61K-000/00; A61K-037/02; A61K-037/24; A61K-039/395; C07K-013/00; C12N-015/00; C12N-015/16; C12P-021/00

6/7/16 (Item 9 from file: 351)
DIALOG(R)File 351:DERWENT WPI

008958583 WPI Acc No: 92-085852/11
XRAM Acc No: C92-039628
Skin external compsn. for accelerating wound healing - contains saiko saponin B1 and/or saiko saponin B2, and cell growth factor
Patent Assignee: (SHIS) SHISEIDO KK
Number of Patents: 001
Number of Countries: 001
Patent Family:

CC Number	Kind	Date	Week	
JP 4029916	A	920131	9211	(Basic)

Priority Data (CC No Date): JP 90134629 (900524)

Abstract (Basic): JP 4029916

Compsn. contains saikosaponin b1 (R = beta-OH) and/or

saiko-saponin b2 (R = alpha-OH) of formula (I), and cell growth factor. In (I), R = beta-OH or alpha-OH.

Pref. combining amt. of saiko-saponin b1 and b2 in total amt. of compsn. is 0.0001-1 wt.% (1-10000 ppm), pref. 0.001-0.1 wt.% (10-1000 ppm). Cell growth factor is e.g. EGF, FGF, PDGF, TGF-beta.

USE/ADVANTAGE - By combination of seco-saponin b1 and/or b2, and cell growth factor, potentiation effect is obtd.. It accelerates healing of wounds, inhibits surface roughening, photodisorder by sunlight, wrinkles, etc.. @(6pp Dwg.No.0/0)@

Derwent Class: B03; D21; E13;
Int Pat Class: A61K-007/00; A61K-031/70; A61K-037/02; A61K-045/06

6/7/17 (Item 10 from file: 351)
DIALOG(R)File 351:DERWENT WPI

008820940 WPI Acc No: 91-324953/44
XRAM Acc No: C91-140339

Pre-disposing mammals to accelerated tissue repair - using transforming growth factor-beta before exposure to tissue damage e.g. wounds, bone fractures prosthetic implants, burns, etc.; RHEUMATISM ARTHRITIS

Patent Assignee: (GETH) GENENTECH INC
Author (Inventor): AMENTO E P; BECK L S
Number of Patents: 008
Number of Countries: 017
Patent Family:

CC	Number	Kind	Date	Week	
WO	9115222	A	911017	9144	(Basic)
US	5108989	A	920428	9220	
EP	527787	A1	930224	9308	
JP	5506030	W	930902	9340	
EP	527787	B1	940302	9409	
DE	69101316	E	940407	9415	
ES	2052378	T3	940701	9429	
WO	9115222	A3	911114	9509	

Priority Data (CC No Date): US 504495 (900404)
Applications (CC,No,Date): WO 91US1861 (910320); EP 91908101 (910320); WO 91US1861 (910320); JP 91507583 (910320); WO 91US1861 (910320); EP 91908101 (910320); WO 91US1861 (910320); DE 601316 (910320); EP 91908101 (910320); WO 91US1861 (910320); EP 91908101 (910320)
Language: English
EP and/or WO Cited Patents: No-Citns.; 4.Jnl.Ref; EP 375127; WO 9100103; NoSR.Pub
Designated States
(National): CA; JP
(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LU; NL; SE; LI
Filing Details: EP0527787 Based on WO 9115222; JP05506030 Based on WO 9115222; EP0527787 Based on WO 9115222; DE69101316 Based on EP 527787; DE69101316 Based on WO 9115222; ES2052378 Based on EP 527787

Abstract (Basic): WO 9115222

A mammal is made capable of accelerated tissue repair by systemically administering transforming growth factor-beta (TGF-beta) prior to exposure to the tissue damage.

The TFG-beta is pref. human TGF-beta.

USE/ADVANTAGE - The method predisposes a mammal to accelerated

wound healing before wound damage occurs and to bone repair prior to a bone fracture, prosthetic implant e.g. hip replacements or bony defect. The tissue damage may also be due to a surgical incision e.g. internal and epidermal incisions and corneal surgery. In general, any form of damage or trauma to soft or hard tissue, including thermally and/or mechanically induced trauma as well as damage caused by inflammatory, infections and immune responses are treated.

Other examples of such tissue damage are 1st, 2nd and 3rd degree burns, wounds e.g. lacerations, incisions and penetrations, sites of possible ulcer development e.g. diabetic, dental, haemophilic, varicose or decubitus ulcers, chronic conditions or ulcers converted to acute wounds, bone infections e.g. osteomyelitis, inflammatory conditions e.g. rheumatoid arthritis and inflammatory conditions leading to bone loss. TGF-beta is administered intravenously in a single dose 5 mins.-24 hrs. before tissue damage exposure. @(22pp Dwg.No.0/3)@

Abstract (US): 9220 US 5108989 A

Stimulating tissue repair in patients awaiting surgery comprises intravenous administratin of beta-tissue growth factors in a single dosage 5 min-24 hrs. before surgery.

USE - Application to patients awaiting surgical incisions, prosthetic implants and the repair of bone defects of fractures.

Abstract (EP): 9409 EP 527787 B

Use of a TGF-beta in the manufacture of a composition for use in a method comprising systemic administration of the composition to a mammal for predisposing the mammal, prior to its exposure to tissue damage, to accelerated tissue repair. Dwg.0/3

Derwent Class: B04;
Int Pat Class: A61K-037/02; A61K-037/24

6/7/18 (Item 11 from file: 351)
DIALOG(R)File 351:DERWENT WPI

008403141 WPI Acc No: 90-290142/38
Related WPI Accession(s): 88-078803; 90-051370; 90-066791; 90-138717; 90-260401; 91-022027; 94-225235
XRAM Acc No: C90-125238

Compsn. for controlled release of bio-active substance - comprises surface-eroding polymer matrix and water-soluble bio-active factors

Patent Assignee: (MASI) MASSACHUSETTS INST TECHNOLOGY
Author (Inventor): DOMB A; GLOWACKI J; LANGER R S; LAURENCIN C T; LUCAS P A ; SYFTESTAD G T; LAURENCIN C
Number of Patents: 003
Number of Countries: 001
Patent Family:

CC	Number	Kind	Date	Week	
WO	9009783	A	900907	9038	(Basic)
US	5356630	A	941018	9441	
US	5545409	A	960813	9638	

Priority Data (CC No Date): US 313953 (890222); US 742264 (910807); US 59516 (930507); US 222880 (940405)
Applications (CC,No,Date): US 313953 (890222); US 742264 (910807); US 59516 (930507)
Language: English
EP and/or WO Cited Patents: 2.Jnl.Ref; WO 8900855
Filing Details: US5545409 Cont of US 5356630

Abstract (Basic): WO 9009783 A

Compsn. for the controlled release of a bioactive substance comprises: a) a shaped matrix sized and adapted for administration of a bioactive substance to an animal and formed of a bioerodable pharmaceutically acceptable material comprising a surface-eroding polym;er; and b) a therapeutically effective amt. of a bioactive substance selected from locally acting factors in the matrix. The compsn. bioerodes at a controlled rate over a period thereby administering the bioactive substance to the animal. Also claimed is a method selectively delivering a bioactive substance to a specific physical site in an animal.

USE/ADVANTAGE - Compsn. and method for controlled administration of the bioactive substance enables successful delivery of the agents with pref. release kinetics and allows soluble agents to interact with local cells. The degradation prods. of the surface-cooling polymers are non-mutagenic, non-cytotoxic and have low feratogenic potential. The compsn. is implanted intramuscularly or subcutaneously and the bioactive substance is selected from TGF-beta, EGF, FGF and PDGF. The method is useful for inducing chondrogenesis and osteogenesis in animsls, and for inducing formation of cartilage and bone in animsls. @(28pp Dwg.No.0/0

Abstract (US): 9638 US 5545409 A

Compsn. for the controlled release of a bioactive substance for inducing formation of cartilage or bone in an animal or wound healing comprises:

a. a shaped matrix sized and adapted for admin. of the bioactive substance to an animal and formed of a polymer selected from polyanhydride and polyorthoester; and

b. a therapeutically effective amt. of a bioactive substance selected from water soluble chondrogenic or osteogenic proteins derived from demineralized bone matrix, TGF-beta, EGF, FGF and PDGF, where the bioactive substance is present at 10-90 wt.% of matrix;

where the compsn. erodes at a controlled rate over a period of time, thereby administering the bioactive substance to the animal in an amt. effective to induce formation of cartilage and bone or wound healing. Dwg.0/0 9441 US 5356630 A

Selective delivery of bioactive substances to induce formation of cartilage and bone and wound healing at a specific site comprises implanting (intramuscularly) at the site a delivery compsn. of shaped matrix formed from 10-90 wt.% surface eroding polyanhydride or polyorthoester polymer and contg. 90-10 wt.% agent, viz. water-sol. chondrogenic or osteogenic proteins derived from demineralised bone, TGF-beta, EGF, FGF, and PDGF. The compsn. erodes hydrolytically at controlled rate over a period releasing proteins at a rate to interact with local cell populations.

ADVANTAGE - Controlled release of bioactive substances at a specific site without general dilution in the body. Dwg.0/0

Derwent Class: A96; B07; B04;
Int Pat Class: A61F-002/28; A61K-009/20; A61K-037/12; A61K-038/39; C07K-014/485; C07K-014/51; C07K-015/20; C07K-017/08

6/7/19 (Item 12 from file: 351)
DIALOG(R)File 351:DERWENT WPI

007976306 WPI Acc No: 89-241418/33
Related WPI Accession(s): 86-022692; 86-346227; 88-292489; 89-093264

XRAM Acc No: C89-107586
Cell proliferation promotion and treatment of osteoporosis - using compsns. contg. cartilage-inducing factors and co-factor
Patent Assignee: (CLGE) COLLAGEN CORP
Author (Inventor): ARMSTRONG R; ELLINGSWOR L; SEYEDIN S; THOMAS T
Number of Patents: 001
Number of Countries: 001
Patent Family:

CC Number	Kind	Date	Week	
US 4843063	A	890627	8933	(Basic)

Priority Data (CC No Date): EP 85304848 (850708)
Applications (CC,No,Date): US 204173 (880608)
Filing Details: US4843063 Continuation 4774322 (+19.8.85, 10.12.87-US-767144, 129864) (1738OM)
Abstract (Basic): US 4843063 A

Promoting cell proliferation comprises admin of a compsn. contg. a beta type transforming growth factor (TGF-beta) activating agent (I), a carrier and a polypeptide (II), the amts. of (I) and (II) being bone growth promoting. (II) has the following characteristics: (a) found in mammalian bone; (b) active in the TGF-beta assay; (c) a co-factor for inducing cartilage formation in vivo; (d) a dimer with mol. wt. 26000 daltons, as determined by SDS-PAGE; and (e) it is pure.

Compsns. of (I) and (II) with an excipient are also claimed for (1) inducing cartilage and bone formation and for repairing, replacing and augmenting cartilage and bone tissue, and (2) treating osteopetrosis by systemic admin.

USE - The cartilage-inducing factors (CIF's), which were isolated from bovine bone (see Parent Patent, US4774322 (88-292489/41)) have in vitro chondrogenic activity by themselves, in vivo chondrogenic activity in combination with certain chondrogenic co-factors in vivo connective tissue deposition activity by themselves and in vitro TGG-beta activity in combination with epidermal growth factor (EGF). Clinical applications of the cell proliferation activity of the compsns. include topical admin. for barn or wound healing or tissue repair. Dwg.0/7

Derwent Class: B04;
Int Pat Class: A61K-009/00; C07G-007/00

6/7/20 (Item 13 from file: 351)
DIALOG(R)File 351:DERWENT WPI

007828152 WPI Acc No: 89-093264/12
Related WPI Accession(s): 86-022692; 86-346227; 88-292489; 89-241418
XRAM Acc No: C89-041391
POlypeptide compsns. for inducing connective tissue deposition, etc. - comprise polypeptide(s) isolated from bone and with activity in beta-type transforming growth factor
Patent Assignee: (CELT-) CELTRIX LAB INC; (CLGE) COLLAGEN CORP
Author (Inventor): ARMSTRONG R; BENTZ H; ELLINGSWORTH L; SEYEDIN S; THOMAS T; ELLINGSWOR L
Number of Patents: 002
Number of Countries: 001
Patent Family:

CC Number	Kind	Date	Week	
US 4810691	A	890307	8912	(Basic)

US RE34090 E 921006 9243

Priority Data (CC No Date): EP 85304848 (850708); US 664762 (910305)
Applications (CC,No,Date): US 131209 (871210); US 630938 (840716); US 767144 (850819); US 131209 (871210); US 129864 (880927)
Filing Details: US0034090 Div ex US 4774322; US0034090 Reissue of US 4810691
Abstract (Basic): US 4810691 A

Compsn. for promoting connective tissue deposition comprises an effective amt. of a polypeptide (I) that: (i) is active in the TGF-beta (beta type transforming growth factor) assay; (ii) is a dimer of mol. wt. ca. 26,000 (by SDS-PAGE) whose chains each have the following N-terminal sequence: Ala-Leu-Asp-Ala-Ala -Tyr-Cys-Phe-Arg-Asn -Val-Gln-Asp-Asn -Cys-Cys-Leu-Arg-Pro-Leu -Tyr-Ile-Asp -Phe-Lys-Arg-Asp-Leu-Gly-Trp-; and (iii) is free of effective amts. of TGF-beta activating agent or chondrogenic co-factor. Compsn. for promoting proliferation of normal animal cells comprises (I) and a TGF-beta activating agent, pref. an EGF or a TGF-alpha. Compsn. for promoting connective tissue deposition comprises an effective amt. of a polypeptide (II) that: (i) is found in mammalian bone; (ii) is active in the TGF-beta assay; (iii) is a co-factor for inducing cartilage formation in vivo; (iv) is a dimer of approx. mol. wt. 26,000 (by SDS-PAGE); and (v) is free of effective amts. of TGF-beta activating agent or chondrogenic co-factor.

USE/ADVANTAGE - Used for promoting corrective tissue deposition without the need for co-factors, or together with co-factors for inducing bone/cartilage formation for repairing, replacing or augmenting bone/cartilage tissue in humans and animals. (I)/(II) may also be useful topically for burn/wound healing or tissue repair, or for treating bone dificiencies (osteoporisis, osteopetrosis), systemically. Dwg.0/7

Abstract (US): 9243 US RE34090 E

Two bone proteins (each M(tan) about 26,000) having in vivo chondrogenic and osteogenic activity in the presence of a cofactor have been isolated. Pharmaceutical compsn. for promoting bone and cartilage growth and/or healing comprises at least one of these proteins, a transforming growth factor activating agent, and the usual carriers and additives.

USE - The prods. promote normal cell growth, esp. for the treatment of bone deficiencies (e.g. osteoporosis and osteopetrosis). Dwg.0/7

Derwent Class: B04;
Int Pat Class: A61K-037/02; C07K-003/28

6/7/21 (Item 14 from file: 351)
DIALOG(R)File 351:DERWENT WPI

004702732 WPI Acc No: 86-206074/32
XRAM Acc No: C86-088539
Application of transforming growth factor-alpha to treat and promote healing of epithelial and stromal wounds
Patent Assignee: (ONCO-) ONCOGEN; (UYLO-) UNIV OF LOUISVILLE
Author (Inventor): TODARO G J; SCHULTZ G L; EIFERMAN R
Number of Patents: 007
Number of Countries: 014
Patent Family:

CC Number	Kind	Date	Week	
EP 190018	A	860806	8632	(Basic)
AU 8652497	A	860807	8638	
JP 61218525	A	860929	8645	
CA 1253071	A	890425	8921	
AU 8947384	A	900503	9024	
EP 190018	B1	930407	9314	
DE 3688203	G	930513	9320	

Priority Data (CC No Date): US 695983 (850129)
Applications (CC,No,Date): DE 3688203 (860124); EP 86300486 (860124); EP 86300486 (860124); JP 8614906 (860128); EP 86300486 (860124)
Language: English
EP and/or WO Cited Patents: 2.Jnl.Ref; A3...8804; EP 105014; EP 132021; EP 154434; No-SR.Pub
Designated States (Regional): AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
Filing Details: DE3688203 Based on EP 190018
Abstract (Basic): EP 190018

The treatment and promotion of healing of epithelial and stromal wounds is effected by applying transforming growth factor-alpha (TGF-alpha) to the region of the wound. A compsn. for this purpose comprises TGF-alpha and a suitable carrier.

The TGF-alpha used is substantially free from contaminants which are naturally present with it. It may be obtd. by purificn. from its natural source or by synthesis, e.g. solid phase synthesis. It is applied topically e.g. in an ointment or as a sterile saline soln., at a concn. e.g. of 1 micro-g/ml to 10 mg/ml. The compsns. may contain other active ingredients, e.g. anaesthetics, antibiotics or antiseptics.

ADVANTAGE - The method is esp. useful for the healing of wounds in the cornea. @(15pp Dwg.No.0/0)@

Abstract (EP): 9314 EP 190018 B

A composition for use in the treatment of epithelial or stromal wounds in the human or animal body comprising transforming growth factor-alpha (TGF-alpha) substantially free from naturally occurring contaminants and from transforming growth factor-beta in a physiologically-acceptable carrier characterised in that the TGF-alpha is a concentration from 50 ng/ml to 10 ml/ml. Dwg.0/0

Derwent Class: B04;
Int Pat Class: A61K-037/02

6/7/22 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

141089 DBA Accession No.: 92-13581 PATENT
Method for accelerated wound healing using new vulnerary composition - topical or parenteral administration of recombinant granulocyte- or granulocyte macrophage-colony stimulating factor, preferably in admixture with e.g. interleukin
PATENT ASSIGNEE: Amgen 1992
PATENT NUMBER: WO 9214480 PATENT DATE: 920903 WPI ACCESSION NO.: 92-315933 (9238)
PRIORITY APPLIC. NO.: US 821498 APPLIC. DATE: 920121
NATIONAL APPLIC. NO.: WO 92US1245 APPLIC. DATE: 920219
LANGUAGE: English

ABSTRACT: A method for promoting accelerated wound healing in an injured patient is claimed, and comprises topical or parenteral administration of a therapeutically effective amount of a colony stimulating factor (CSF) selected from granulocyte-CSF (G-CSF) or granulocyte macrophage-CSF (GM-CSF). The CSF is made by recombinant methods, using eukaryotic or prokaryotic cells, especially Escherichia coli. The recombinant CSF is preferably used in admixture with at least 1 other protein selected from recombinant epidermal growth factor, fibroblast growth factor, G-CSF, GM-CSF, somatomedin-C, insulin-like growth factor-2, insulin, an interferon (-alpha, -beta or -gamma), an interleukin (-1, -2, -3, -4, -5, -6, -7, -8, -9 or -10), keratinocyte growth factor, platelet-derived endothelial cell growth factor, platelet-derived growth factor, stem cell factor, transforming growth factor (TGF)-alpha and TGF-beta. The admixture is administered in a formulation selected from collagen-based creams, films, microcapsules, powders, hyaluronic acid or other glycosaminoglycans, etc. Mechanical, thermal, acute, chronic, infected or sterile wounds can be healed. (46pp)

6/7/23 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

041283 DBA Accession No.: 85-12072 PATENT
New DNA encoding human transforming growth factor precursor - for production of precursor for treatment of bone diseases and to accelerate wound healing
PATENT ASSIGNEE: Genentech 1985
PATENT NUMBER: EP 154434 PATENT DATE: 850911 WPI ACCESSION NO.: 85-224827 (8537)
PRIORITY APPLIC. NO.: US 695494 APPLIC. DATE: 850211
NATIONAL APPLIC. NO.: EP 85301037 APPLIC. DATE: 850215
LANGUAGE: English
ABSTRACT: A process is described for the production of human transforming growth factor-alpha (TGF-alpha) precursor and its fragments by recombinant DNA technology. The process involves incorporating a DNA fragment coding for TGF-alpha precursor into a vector and using the recombinant vector to transform suitable microorganism hosts, e.g. Escherichia coli, for the production of TGF-alpha precursor. High purity TGF-alpha-precursor is obtained in sufficient quantities for use as a therapeutic agent in patients with bone diseases and to accelerate wound healing. TGF-alpha is useful as an adjuvant for cell culture to reduce the serum requirement of the medium, with advantages in the purification of products, and to stimulate or enhance cell growth during culture. TGF-alpha precursor and its fragments permit the preparation of antibody for use in assay of the precursor and its fragments in body fluids for the diagnosis of neoplastic and other diseases. Preferably, the TGF-alpha precursor is mutated and compositions may be conjugated to a heterologous polypeptide heterologous to the organism from which the DNA encoding the precursor was obtained. (72pp)
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          OneSearch, 7 files,  0.100 Hrs FileOS
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IF YOU REQUIRE FURTHER HELP, PLEASE CONTACT YOUR LOCAL HELP DESK
=> s wound?
L2 151582 WOUND?

=> s heal?
L3 72514 HEAL?

=> s fgf
L4 753 FGF

=> s l1(P)l2(P)l3
L5 13 L1(P)L2(P)L3

=> s l4(P)l3(P)l2
L6 173 L4(P)L3(P)L2

=> s l6(P)l1
L7 1 L6(P)L1

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1. 5,662,904, Sep. 2, 1997, Anti-scarring compositions comprising growth factor neutralizing antibodies; Mark William James Ferguson, et al., 424/130.1, 145.1; 530/387.1, 388.24, 391.1, 391.7 :IMAGE AVAILABLE:

US PAT NO: 5,662,904 :IMAGE AVAILABLE: L7: 1 of 1

SUMMARY:

BSUM(5)

In adult humans and other mammalian vertebrates, **wound healing** in tissues such as skin is generally a reparative process, in contrast to a regenerative process which appears to take place in **healing** of fetal and embryonic tissue. The outcome of a **wound** repair process appears no be influenced by a number of different factors, including both intrinsic parameters, e.g. tissue oxygenation; and extrinsic parameters, e.g. **wound** dressings. There is, however, considerable evidence indicating that the overall process of **healing** and repair of **wound** damaged tissue, including the necessary innercellular communication, is regulated in a coordinated manner in adult humans and other mammals by a number of specific soluble growth factors which are released within the **wound** environment (especially by degranulating platelets and incoming macrophages) and which, amongst other things, appear to induce neovascularisation, leucocyte chemotaxis, fibroblast proliferation, migration and deposition of collagen and other extracellular matrix molecules within the **wounds**. Such growth factors that have been identified and isolated are generally specialised soluble proteins or polypeptides and include transforming growth factor alpha (TGF-.alpha.), transforming growth factor **beta** (**TGF**-.**beta**.1, **TGF**-.**beta**.2, **TGF**-.**beta**.3 etc), platelet derived growth factor (PDGF), epidermal growth factor (EGF), insulin-like growth factors I and II (IGFI and IGFII) and acidic and basic fibroblast growth factors (acidic **FGF** and basic **FGF**). Many of these growth factors have already been made by genetic engineering using recombinant DNA technology.

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